Int J Cancer Manag. 2022 October; 15(10):e123887. doi: 10.5812/ijcm-123887.

Published online 2022 October 4. **Research Article**

COVID-19 Breakthrough Infections Among Patients with Cancer Receiving Sinopharm BBIBP-CorV Vaccine

Amirreza Manteghinejad [1], Saeedeh Arabzadeh [1], Zahra Rezaian [1], Mehran Sharifi [2, 1, *] and Shaghayegh Haghjooy Javanmard [3]

[1] Cancer Prevention Research Center, Omid Hospital, Isfahan University of Medical Sciences, Isfahan, Iran
[2] Hematology and Oncology Division, Department of Internal Medicine, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran
[3] Applied Physiology Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran

[*] *Corresponding author*: Cancer Prevention Research Center, Omid Hospital, Isfahan, Iran. Email: mehransharifi147@med.mui.ac.ir

Received 2022 March 06; **Revised** 2022 August 10; **Accepted** 2022 September 20.

Abstract

Background: Patients with cancer are at an increased risk of mortality from COVID-19 infection. So, they are prioritized for vaccination. However, there is limited data about the immunogenicity, safety, and effectiveness of inactivated vaccines in preventing COVID-19 infection, hospitalization, and mortality in patients with cancer.
Objectives: This study aimed to report the clinical characteristics of patients who had a positive PCR test after being fully vaccinated with the Sinopharm BBIBP-CorV Vaccine.
Methods: In this retrospective study, the data of patients with cancer were extracted from the electronic health records of a cancer center in Isfahan, Iran. All COVID-19 data from Isfahan province also was collected by Isfahan COVID-19 Registry (I-CORE). We described the clinical characteristics of patients with cancer who have a positive test more than 14 days after the second dose.
Results: Two hundred twenty-two patients with cancer had at least one positive PCR test after the start of the COVID-19 vaccination. Of these, 9 (4.1%) breakthrough infections have occurred. Six (67%) of them had hematological malignancies. Six (67%) were hospitalized and 3 (33%) patients died. Two of them had recent chemotherapy and have hematological malignancies.
Conclusions: Vaccination is a good way to protect the population from COVID-19 complications and mortality, but it should be considered that fully-vaccinated patients with cancer are at risk of severe outcomes. Nevertheless, prioritizing cancer patients, especially those with hematological malignancies, or receiving chemotherapies for booster vaccines and studying the effectiveness of each COVID-19 vaccine for patients with cancer should be considered.

Keywords: COVID-19, Cancer, Vaccination, COVID 19 Vaccines, COVID-19 Breakthrough

1. Background

Since the beginning of the COVID-19 pandemic, patients with cancer have faced several challenges (1). Up to now, we know that patients with cancer are at a high risk of mortality from COVID-19 infection (2, 3). Consequently, they are prioritized for vaccination since it is the most effective way of preventing the disease (4, 5). However, the immune impairments which result from cancer itself or the therapeutics for cancers can affect the vaccine effectiveness (6). To date, there are limited studies about the immunogenicity, safety, and efficacy of inactivated vaccines in preventing COVID-19 infection, hospitalization, and mortality in patients with cancer. A study by Ariamanesh et al. showed that the seroconversion rate in cancer patients receiving the Sinopharm BBIBP-CorV vaccine is 86.9% (7). However, this study did not report any breakthrough infections. Another study by Joudi et al. also found that the seroconversion rate in patients with breast cancer receiving the Sinopharm BBIBP-CorV vaccine is more than 80%, and the breakthrough infection rate is 0.7% (8).

2. Objectives

The aim of this study was to report the patients' demographics, clinical characteristics, and outcomes of all the patients with any type of cancer at a tertiary referral cancer center who had a positive PCR test after they were fully vaccinated by the Sinopharm BBIBP-CorV COVID-19 vaccine.

3. Methods

3.1. Data Acquisition

Omid cancer hospital is a tertiary referral cancer center affiliated with the Isfahan University of Medical Sciences, also known as Medical University of Isfahan (MUI) in Isfahan, Iran. The data of patients with cancer who reside in Isfahan Province was extracted from the hospital information system (HIS).

The data of patients with a positive SARS-CoV-2 PCR from 21 February 2020 until 16 August 2021 was also gathered by Isfahan COVID-19 Registry (I-CORE) (9). Vaccination status data was also collected by I-CORE.

The data of these two datasets were linked together using the national identification number. We identified breakthrough infections in fully vaccinated patients, defined as a positive test > 14 days after the second vaccine dose (10).

After finding the patients with breakthrough infections, clinical characteristics, comorbidities, signs, and symptoms were extracted from the electronic and paper health records.

3.2. Statistical Analysis

Preprocessing of data was done in Python using Pandas and NumPy libraries. Afterward, data were entered into Statistical Package for the Social Sciences (SPSS) Statistics software version 26. Median with Interquartile range (IQR) and frequency were used to report categorical and continuous variables.

3.3. Ethics Approval

This study was approved by the Research Ethics Committees of Vice-Chancellor in Research, Medical University of Isfahan (Approval ID: IR.MUI.MED.REC.1400.483).

4. Results

A total of 495 Patients with cancer have had a positive PCR test since 21 February 2020, the day that the first patient with cancer was diagnosed with COVID-19; 222 of them were after the start of COVID-19 vaccination in Iran. Of these, 9 (4.1%) breakthrough infections have occurred (Figure 1). Among them, 6 (67%) were male with a median age of 64, and 6 (67%) had at least one comorbidity besides cancer. Six (67%) have hematological malignancies (Table 1).

All the patients received the Sinopharm BBIBP-CorV vaccine. Eight (88.9%) patients were symptomatic, and 6 (67%) were hospitalized. The median time from the final vaccine dose to infection was 60 days. At last, 3 (33%) of the patients died. Two of them had recent chemotherapy and hematological malignancy. The chemotherapy regimen of one of these patients included rituximab, and the other one received bortezomib and lenalidomide. The information about these patients is available in Table 2.

5. Discussion

Findings showed that a small portion (4.1%) of patients with cancer in our center were infected with COVID-19 when fully vaccinated. As previous studies showed that the seroconversion rate of the Sinopharm BBIBP-CorV vaccine is more than 80% (7, 8), it seems that the Sinopharm vaccine is an effective method for preventing COVID-19. Other studies also reported the limited number of breakthrough infections in the general population and showed that breakthrough infection is correlated with neutralizing antibody titers (11, 12). There is only a limited number of studies describing breakthrough infections in patients with cancer. A study by Schmidt et al. showed that cancer patients with hematological malignancies are at more risk for breakthrough infections (13). Another study by Pagano et al. described breakthrough infections in patients with hematological malignancies also showed that breakthrough infections are more prevalent in patients with lymphoproliferative malignancies (14). Our findings also show that breakthrough infections are more prevalent in patients with lymphoproliferative malignancies and mortality is more prevalent in cancer patients under active chemotherapy.

Multiple myeloma and mantle cell lymphoma are lymphoid disorders that affect the B cells. As the Sinopharm BIPP vaccine mechanism of action relies on producing neutralizing antibodies (15), it seems that these patients are at increased risk of reinfection.

One of the patients who died received rituximab. A study by Bonelli et al. also showed impaired humoral response after COVID-19 vaccination in patients receiving rituximab (16). It is not surprising that Anti-CD20 antibodies, which deplete the B cells, predispose patients to infections.

5.1. Limitations

This study had several limitations. First, this study was conducted during a period when cancer patients did not

Table 1. Patient Characteristics, Cancer Details, and Infection Details of COVID-19 Breakthrough Infections in Fully Vaccinated Patients with Cancer (N = 9)

Patient Characteristics	No. (%)
Gender	
Male	6 (66.7)
Female	3 (33.3)
Age (median, IQR)	64 (58 - 74)
Type of cancer	
Hematological	6 (66.7)
Solid tumor	3 (33.3)
Hematological cancers	
Multiple myeloma	2 (22.2)
Acute myeloblastic leukemia	1 (11.1)
Mantle cell lymphoma	1 (11.1)
Hodgkin lymphoma	1 (11.1)
Non-hodgkin lymphoma	1 (11.1)
Solid tumors	
Breast	1 (11.1)
Thyroid	1 (11.1)
Connective Tissue	1 (11.1)
Comorbidities	
Hypertension	3 (33.3)
Other cardiovascular diseases	2 (22.2)
Diabetes	2 (22.2)
Chronic kidney disease	2 (22.2)
Dialysis	1 (11.1)
Cancer Treatments	
Recent chemotherapy (within four weeks of admission)	3 (33.3)
Days from second vaccine dose to infection (median, IQR)	60 (56 - 69)
Have any symptoms	
Yes	8 (88.9)
No	1 (11.1)
Symptoms	
Fever	6 (66.7)
Cough	6 (66.7)
Dyspnea	5 (55.5)
Malaise	7 (77.8)
Myalgia	6 (66.7)
Headache	1 (11.1)
Diarrhea/vomiting/nausea	3 (33.3)
Anosmia	3 (33.3)
Dysgeusia	2 (22.2)
Chest Pain	3 (33.3)
Outcomes	
Outpatient only	3 (33.3)
Hospitalization	6 (66.6)
Death	3 (33.3v

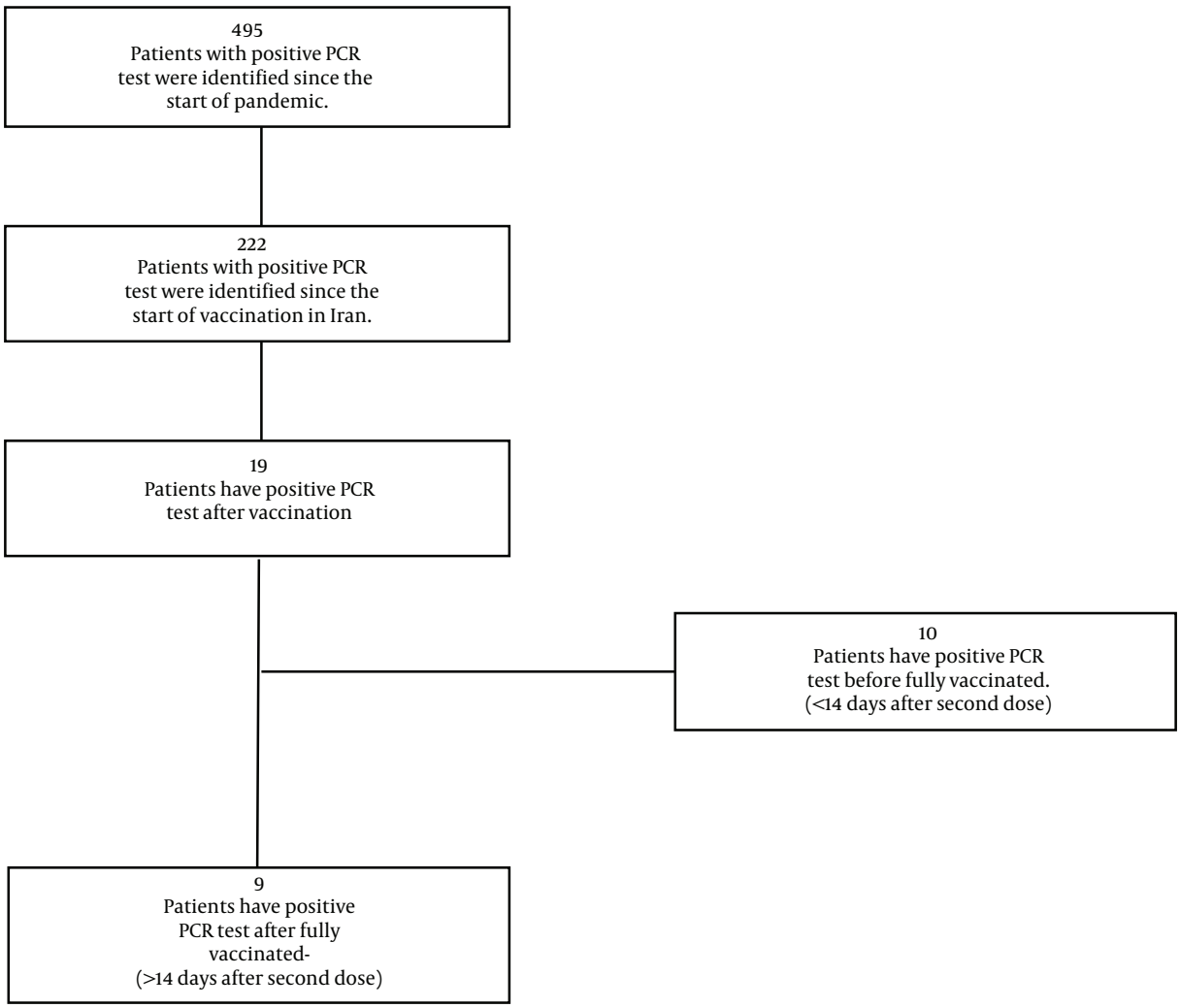

Figure 1. Identification of COVID-19 breakthrough infections among vaccinated patients with cancer

receive booster doses. As the booster doses could affect these results, it is highly suggested that other studies describe the breakthrough infections after the booster doses. Moreover, in this study, we did not evaluate the presence of SARS-CoV2 antibodies. Finally, it is worth mentioning that we used a registry database for obtaining the PCR results, and this registry did not record the details of COVID-19 diagnostic kits. As the sensitivity of different kits may differ, it could affect the PCR tests.

5.2. Conclusions

Our study also showed that, although vaccination reduces the chance of getting infected, more than half of cancer patients with breakthrough infection were hospitalized, and a third finally died. This might be because of the emergence of new virus variants or the difference in the effectiveness of vaccines in cancer patients for preventing hospitalization or mortality.

The authors suggest that it is necessary to study the effectiveness of each COVID-19 vaccine for cancer patients to find the best vaccine for these patients. Moreover, Because of the waning immunity of vaccines especially inactivated vaccines, patients with cancer received booster doses to prevent COVID-19 infection (17). As a result, conducting studies comparing the effectiveness of booster vaccines especially those with hematological malignancies or receiving chemotherapies, is highly suggested.

Table 2. The Brief Dataset of COVID-19 Breakthrough Infections Among Vaccinated Patients with Cancer

Case	Age	Cancer Type	Time from Final Vaccine to Diagnosis (d)	Recent Chemotherapy	Asymptomatic Infection	Hospitalization	Deceased
1	56	Acute myeloblastic leukemia	43	No	Yes	No	No
2	64	Multiple myeloma	69	Yes	No	Yes	Yes
3	73	Mantle cell lymphoma	61	Yes	No	Yes	Yes
4	74	Malignant neoplasm of breast	44	No	No	No	No
5	32	Hodgkin lymphoma	83	Yes	No	Yes	No
6	58	Multiple myeloma	60	No	No	Yes	No
7	75	Non-hodgkin lymphoma	56	No	No	Yes	No
8	78	Malignant neoplasm of connective and soft tissue	83	No	No	No	No
9	64	Malignant neoplasm of thyroid	60	No	No	Yes	Yes

Acknowledgments

The authors wish to thank all associated healthcare providers and hospital staff of Omid Hospital for their pure services and cooperation during COVID-19.

Footnotes

Authors' Contribution: AM, SH, and MS performed the study concept and design. AM, SA, and ZR were involved in data acquisition. AM wrote the first draft of the manuscript. All authors contributed to the critical revision and final approval of this manuscript.

Conflict of Interests: The authors declare that they have no competing interests.

Data Reproducibility: The brief dataset of the study is available in Table 2; a de-identified detailed version will be made available from the corresponding author upon reasonable request.

Ethical Approval: This study was approved by the Research Ethics Committees of Vice-Chancellor in Research, Medical University of Isfahan (Approval ID: IR.MUI.MED.REC.1400.483).

Funding/Support: This research received no specific grant from public, commercial, or not-for-profit funding agencies.

References

1. Fadavi P, Houshyari M, Yousefi Kashi AS, Jarrahi AM, Roshanmehr F, Broomand MA, et al. Review on the Oncology Practice in the Midst of COVID-19 Crisis: The Challenges and Solutions. *Asian Pac J Cancer Prev*. 2021;**22**(1):19–24. doi: 10.31557/APJCP.2021.22.1.19. [PubMed: 33507674]. [PubMed Central: PMC8184167].
2. ElGohary GM, Hashmi S, Styczynski J, Kharfan-Dabaja MA, Alblooshi RM, de la Camara R, et al. The risk and prognosis of COVID-19 infection in cancer patients: A systematic review and meta-analysis. *Hematol Oncol Stem Cell Ther*. 2020. doi: 10.1016/j.hemonc.2020.07.005. [PubMed: 32745466]. [PubMed Central: PMC7390725].
3. Taghizadeh-Hesary F, Porouhan P, Soroosh D, PeyroShabany B, Shahidsales S, Keykhosravi B, et al. COVID-19 in Cancer and Non-cancer Patients. *Int J Cancer Manag*. 2021;**14**(4). doi: 10.5812/ijcm.110907.
4. Ribas A, Sengupta R, Locke T, Zaidi SK, Campbell KM, Carethers JM, et al. Priority COVID-19 Vaccination for Patients with Cancer while Vaccine Supply Is Limited. *Cancer Discov*. 2021;**11**(2):233–6. doi: 10.1158/2159-8290.CD-20-1817. [PubMed: 33355178]. [PubMed Central: PMC8053003].
5. Griffiths EA, Segal BH. Immune responses to COVID-19 vaccines in patients with cancer: Promising results and a note of caution. *Cancer Cell*. 2021;**39**(8):1045–7. doi: 10.1016/j.ccell.2021.07.001. [PubMed: 34242573]. [PubMed Central: PMC8253695].
6. Abdul-Jawad S, Bau L, Alaguthurai T, Del Molino Del Barrio I, Laing AG, Hayday TS, et al. Acute Immune Signatures and Their Legacies in Severe Acute Respiratory Syndrome Coronavirus-2 Infected Cancer Patients. *Cancer Cell*. 2021;**39**(2):257–275 e6. doi: 10.1016/j.ccell.2021.01.001. [PubMed: 33476581]. [PubMed Central: PMC7833668].
7. Ariamanesh M, Porouhan P, PeyroShabany B, Fazilat-Panah D, Dehghani M, Nabavifard M, et al. Immunogenicity and Safety of the Inactivated SARS-CoV-2 Vaccine (BBIBP-CorV) in Patients with Malignancy. *Cancer Invest*. 2022;**40**(1):26–34. doi: 10.1080/07357907.2021.1992420. [PubMed: 34634986]. [PubMed Central: PMC8567287].
8. Joudi M, Moradi Binabaj M, Porouhan P, PeyroShabany B, Tabasi M, Fazilat-Panah D, et al. A Cohort Study on the Immunogenicity and Safety of the Inactivated SARS-CoV-2 Vaccine (BBIBP-CorV) in Patients With Breast Cancer; Does Trastuzumab Interfere With the Outcome? *Front Endocrinol (Lausanne)*. 2022;**13**:798975. doi: 10.3389/fendo.2022.798975. [PubMed: 35299966]. [PubMed Central: PMC8923352].

9. Javanmard SH, Nasirian M, Ataei B, Vaseghi G, Vaezi A, Changiz T. Isfahan COvid-19 REgistry (I-CORE): Design and methodology. *J Res Med Sci*. 2020;**25**:32. doi: 10.4103/jrms.JRMS_271_20. [PubMed: 32582338]. [PubMed Central: PMC7306237].
10. Moline HL, Whitaker M, Deng L, Rhodes JC, Milucky J, Pham H, et al. Effectiveness of COVID-19 Vaccines in Preventing Hospitalization Among Adults Aged >/=65 Years - COVID-NET, 13 States, February-April 2021. *MMWR Morb Mortal Wkly Rep*. 2021;**70**(32):1088–93. doi: 10.15585/mmwr.mm7032e3. [PubMed: 34383730]. [PubMed Central: PMC8360274].
11. Juthani PV, Gupta A, Borges KA, Price CC, Lee AI, Won CH, et al. Hospitalisation among vaccine breakthrough COVID-19 infections. *Lancet Infect Dis*. 2021;**21**(11):1485–6. doi: 10.1016/S1473-3099(21)00558-2. [PubMed: 34506735]. [PubMed Central: PMC8423430].
12. Bergwerk M, Gonen T, Lustig Y, Amit S, Lipsitch M, Cohen C, et al. Covid-19 Breakthrough Infections in Vaccinated Health Care Workers. *N Engl J Med*. 2021;**385**(16):1474–84. doi: 10.1056/NEJMoa2109072. [PubMed: 34320281]. [PubMed Central: PMC8362591].
13. Schmidt AL, Labaki C, Hsu CY, Bakouny Z, Balanchivadze N, Berg SA, et al. COVID-19 vaccination and breakthrough infections in patients with cancer. *Ann Oncol*. 2022;**33**(3):340–6. doi: 10.1016/j.annonc.2021.12.006. [PubMed: 34958894]. [PubMed Central: PMC8704021].
14. Pagano L, Salmanton-Garcia J, Marchesi F, Lopez-Garcia A, Lamure S, Itri F, et al. COVID-19 in vaccinated adult patients with hematological malignancies: preliminary results from EPICOVIDEHA. *Blood*. 2022;**139**(10):1588–92. doi: 10.1182/blood.2021014124. [PubMed: 34748627]. [PubMed Central: PMC8577877].
15. Al Kaabi N, Zhang Y, Xia S, Yang Y, Al Qahtani MM, Abdulrazzaq N, et al. Effect of 2 Inactivated SARS-CoV-2 Vaccines on Symptomatic COVID-19 Infection in Adults: A Randomized Clinical Trial. *JAMA*. 2021;**326**(1):35–45. doi: 10.1001/jama.2021.8565. [PubMed: 34037666]. [PubMed Central: PMC8156175].
16. Bonelli MM, Mrak D, Perkmann T, Haslacher H, Aletaha D. SARS-CoV-2 vaccination in rituximab-treated patients: evidence for impaired humoral but inducible cellular immune response. *Ann Rheum Dis*. 2021;**80**(10):1355–6. doi: 10.1136/annrheumdis-2021-220408. [PubMed: 33958323].
17. Croda J, Ranzani OT. Booster doses for inactivated COVID-19 vaccines: if, when, and for whom. *Lancet Infect Dis*. 2022;**22**(4):430–2. doi: 10.1016/S1473-3099(21)00696-4. [PubMed: 34890538]. [PubMed Central: PMC8651253].