

Prevalence of covid-19 breakthrough after vaccination and adverse effects of vaccines

Fatima Ehsan,¹ Fouzia Hanif,² Qudsia Ishaq,³ Maleha Asim,⁴ Maria Yousaf,⁵ Aqeel Mansoor⁶

¹Department of Endocrinology and Diabetes, Riphah International University, ²Department of Medicine, ³Department of Biochemistry, Federal Medical and Dental College, ⁴Department of Medicine, RIU, ⁵Department of Biochemistry, Bilal Hospital, ⁶Department of Physiology, RIU, Islamabad, Pakistan

Objective: To assess the prevalence of breakthrough Covid 19 after vaccination and adverse effects of vaccines.

Methodology: This descriptive cross-sectional study was conducted at three mega vaccination centers in Islamabad from December 1, 2021, to May 1, 2022. The sample size consisted of 300 participants in the age range of 30-60 years. We included only those participants who were fully vaccinated. Among these, 150 were healthy individuals and 150 had comorbidities, were selected through convenience sampling. Data were analyzed using SPSS version 21.

Results: A significant association between breakthrough COVID-19 and age and symptoms were

found in fully vaccinated individuals with and without comorbidities. The type of vaccine had a significant association only in individuals without medical illness. No significant side effects of the vaccine or gender association were found in either group. We also found a significant association between breakthrough COVID-19 symptoms and the type of vaccine used.

Conclusion: A significant association between vaccine type and breakthrough COVID was observed only in healthy individuals, probably because of their different mechanisms of action.

Keywords: Vaccines, Pakistan, comorbidities, Covid 19.

INTRODUCTION

The SARS-CoV-2 virus is the cause of the respiratory illness known as COVID-19 or coronavirus disease.¹ It has severely impacted society and the economy, upsetting daily life.² In late 2020, the vaccine was made available to the public to curb widespread COVID-19. There was clear evidence of benefits, as indicated by decreased infectivity in post-vaccination phases.³

According to the CDC, a “breakthrough” infection occurs in individuals who have detectable SARS-CoV-2 RNA or antigen on respiratory specimens collected ≥ 14 days post-vaccination.⁴ Although available vaccines have remarkable efficacy in preventing severe forms of COVID-19, they cannot efficiently prevent transmission.^{5,6} Moreover, these vaccines confer infection-permissive or “non-sterilizing” immunity, which may permit infection while preventing symptoms, particularly severe symptoms.⁷

Post-vaccination cases of COVID-19 do occur, suggesting a lack of vaccine effectiveness.⁸ Although any fully vaccinated person can experience a breakthrough infection, people with weakened immune systems caused by certain medical conditions or treatments (including organ transplants, HIV and some cancers and chemotherapy) are more likely to have breakthrough infections.⁹ In Pakistan, two common types of vaccines

are either mRNA vaccines (Pfizer, Moderna) or the more common vector vaccine (Sino pharm, Sino vac, Astra Zeneca). Although the mechanisms are different, both build immunity against this SARS-Covid virus.¹⁰

As it is important to administer safe and effective COVID-19 vaccinations, there is less real-world data available in Pakistan about breakthrough cases in fully COVID-19-vaccinated people, even in individuals with comorbidities. Analyses of such clinical outcomes of breakthrough cases could be an important supplement to the observational effectiveness data of COVID-19 vaccines in Pakistan. The aim of this study was to assess the prevalence of breakthrough Covid 19 after vaccination and adverse effects of vaccines.

METHODOLOGY

This questionnaire-based study was conducted on a sample of 300 males and females with ages ranging from 30 to 60 years. Participants were interviewed from three mega vaccination centres in Islamabad and Rawalpindi. Only those participants who were fully vaccinated were included. Two groups, including 150 healthy individuals and 150 with co-morbidities were selected through serial techniques of sampling. The research proposal approval was obtained from the institutional ethical committee (Ref: FMTI ERRB/ 15/07 dated November 1, 2021) and

an Informed consent was obtained from all participants.

Statistical Analysis: A group of volunteers consisting of three male and two female members helped in the data collection. To ensure easy and rapid retrieval of the data, manually prepared information sheets of data were entered on MS Excel sheets. The chi-square test of independence was performed to assess the dependency of breakthrough COVID-19. The data analysis was performed using SPSS v. 21.

RESULTS

Out of 300 participants, 126(42%) were males and 174(58%) females. Age range was from 30 to 39 to over 60 years (Table 1). No association of gender was found among the vaccinated individuals. Regarding the symptoms among vaccinated individuals, there was a significant association. The majority of vaccinated individuals with medical illness fell into the moderate category of symptoms, whereas those without fell into mild symptoms.

There was no association between vaccine type and breakthrough COVID among individuals with medical illness, whereas there was a significant association with vaccine type among vaccinated individuals without medical illness. From the latter group, those who did not get breakthrough COVID had the Pfizer vaccine mostly and those who got COVID had the Sino Pharm vaccine mostly. There were no significant side effects of the vaccine in either group. Regarding whether precautionary measures were continued even after vaccination, we found a significant association only among those with medical illness. However, regarding the perception and advocacy of vaccination, we found a significant association in individuals with no medical illness (Table 2).

DISCUSSION

In our study, a significant association of breakthrough COVID cases was found with age, with the majority falling into the 50–59 years group regardless of having comorbidities or not. This is similar to a study from

Table 1: Breakthrough Covid-19 in vaccinated patients with medical illness.

Participant characteristics	No breakthrough (n=115)	Breakthrough (n=35)	p value
Age			0.002
30-39	15 (13.0%)	02 (5.7%)	
40-49	57 (49.6%)	08 (22.9%)	
50-59	35 (30.4%)	17 (48.6%)	
Over 60	08 (7.0%)	08 (22.9%)	
Gender			0.64
Males	54 (47.0%)	18 (51.4%)	
Females	61 (53.0%)	17 (48.6%)	
Symptoms of COVID-19			<0.001
None	121 (100%)	07 (24.1%)	
Mild	0 (0.0%)	01 (3.4%)	
Moderate	0 (0.0%)	20 (69.0%)	
Severe	0 (0.0%)	01 (3.4%)	
Type of Vaccine			0.92
AstraZeneca	07 (6.1%)	02 (5.7%)	
Can Sino	05 (4.3%)	03 (8.6%)	
Moderna	05 (4.3%)	02 (5.7%)	
Pfizer	28 (24.3%)	07 (20.0%)	
Sino Pharm	47 (40.9%)	15 (42.9%)	
Sino Vac	23 (20.0%)	06 (17.1%)	
Side effects of Vaccine			0.23
Fever	12 (10.4%)	08 (22.9%)	
Body aches	19 (16.5%)	08 (22.9%)	
Chills/Rigors	17 (14.8%)	06 (17.1%)	
Headache	16 (13.9%)	02 (5.7%)	
Flu like symptoms	17 (14.8%)	05 (14.3%)	
None	34 (85.0%)	06 (17.1%)	

Tunisia, where the average age of the overall breakthrough cases was 55.7 years. However, they also had a significant association with the female gender, whereas no such association was found in this study.¹¹

Vaccination trials were conducted in Europe, the United States, Australia, and China; therefore, data are scarce in this context. In our study, no significant association was

found with acute side effects of the vaccine, even in individuals with a clinical history of chronic diseases irrespective of their mechanism of action. This is contrary to another study conducted by the Fauji Foundation, in which the clinical history of comorbidities was significantly associated with the development of post-vaccination side effects. However, that study focused entirely on side effects and compared side effects with individual diseases, such as diabetes and hypertension, where it was significantly associated with headache ($p<0.001$) and fatigue ($p=0.002$) in hypertensive patients.¹²

The majority of patients experienced no side effects in our study. Studies have shown that vaccine side effects should not be taken as a measure of the effectiveness of the vaccine. Despite the varied immune response to vaccines, most people achieve immunity against coronavirus on vaccination, regardless of the presence, absence, or severity of side effects.¹³

When comparing the type of vaccine with breakthrough cases, a significant association was observed regarding vaccine type in fully vaccinated individuals with the highest breakthrough COVID cases with Sino pharm, whereas the Pfizer vaccine was on top among vaccines and presented no breakthrough COVID cases. No such associations were observed in individuals with comorbidities most probably because of their already compromised immune systems. However, because this was a cross-sectional study conducted over a limited period, we cannot comment on the long-term effects of these vaccines. Brunelli et al detected no difference in the efficacy of vaccines generally within the first 6 months after vaccination in a cohort of dialysis patients.¹⁴ Regarding the severity of symptoms of breakthrough COVID cases in fully vaccinated individuals, we categorized them into no symptoms, mild, moderate, and severe (hospitalization). The majority fell into the moderate category among those with comorbidities and the mild category in apparently healthy individuals. Immunocompromising conditions such as diabetes could weaken the antibody response to vaccination, which may explain the association with the severity of symptoms in

Table 2: Breakthrough Covid-19 in vaccinated patients with no medical illness.

Participant characteristics	No breakthrough (n=115)	Breakthrough (n=35)	p value
Age			<0.001
30-39	34 (28.1%)	02 (6.9%)	
40-49	71 (58.7%)	06 (20.7%)	
50-59	13 (10.7%)	15 (51.7%)	
Over 60	03 (2.5%)	06 (20.7%)	
Gender			0.80
Males	43 (35.5%)	11 (37.9%)	
Females	78 (64.5%)	18 (62.1%)	
Symptoms of COVID-19			
None	115 (100%)	10 (6.7%)	<0.001
Mild	0 (0.0%)	20 (57.1%)	
Moderate	0 (0.0%)	02 (5.7%)	
Severe	0 (0.0%)	03 (8.6%)	
Type of Vaccine			0.002
AstraZeneca	0 (0.0%)	20 (57.1%)	
Can Sino	0 (0.0%)	02 (5.7%)	
Moderna	0 (0.0%)	03 (8.6%)	
Pfizer	115 (100%)	10 (6.7%)	
Sino Pharm	0 (0.0%)	20 (57.1%)	
Side effects of Vaccine			0.10
Fever	17 (14.0%)	05 (17.2%)	
Body aches	10 (8.3%)	06 (20.7%)	
Chills/Rigors	03 (2.5%)	03 (10.3%)	
Headache	06 (5.0%)	01 (3.4%)	
Flu like symptoms	01 (0.8%)	00 (0.0%)	

this study. Galmiche et al reported a higher prevalence of the severe breakthrough delta variant of COVID among patients with CVD, diabetes, and other immunocompromised conditions.¹

We also correlated these breakthrough COVID symptoms among all fully vaccinated individuals with the type of vaccine and found a significant association ($p<0.04$) irrespective of co-morbidities. Most of the various vaccines resulted in symptoms that were either none or mild, which is consistent with the findings of another study.¹⁶ In our study, Sino pharm had the highest

percentage of all categories of symptoms in addition to Moderna, which also had the highest percentage of symptoms in the moderate category.

This study had a few limitations, such as a small sample size, single geographic location and exclusion of young and older populations.

CONCLUSION

Symptoms of breakthrough COVID-19 in individuals with comorbidities were moderate compared to mild symptoms in apparently healthy and fully vaccinated individuals due to the protective effects of the vaccine. There was a significant association between vaccine type and breakthrough COVID-19 only in healthy individuals, probably due to different mechanisms of action.

Author Contributions:

Conception and design: Fatima Ehsan, Qudsia Ishaq.
Collection and assembly of data: Fatima Ehsan, Maria Yousaf.
Analysis and interpretation of the data: Fouzia Hanif, Qudsia Ishaq.
Drafting of the article: Maleha Asim.
Critical revision of the article for important intellectual content: Aqeel Mansoor.

Statistical expertise: Maleha Asim.

Final approval and guarantor of the article: Aqeel Mansoor.

Corresponding Author Email: Fatima Ehsan:

fatima.ehsan@riphah.edu.pk

Conflict of Interest: None declared.

Rec. Date: Oct 12, 2023 Revision Rec. Date: Mar 3, 2024 Accept Date: Mar 26, 2024.

REFERENCES

1. Zhou P, Yang X-L, Wang X-G, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*. 2020;579(7798):270–3.
2. Yin Y, Wunderink RG. MERS, SARS and other coronaviruses as causes of pneumonia. *Respirology*. 2018;23:130–137.
3. Hui DS, I Azhar E, Madani TA, Ntoumi F, Kock R, Dar O, et al. The continuing 2019-ncov epidemic threat of novel coronaviruses to Global Health — the latest 2019 novel coronavirus outbreak in Wuhan, China. *International Journal of Infectious Diseases*. 2020;91:264–6.
4. Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. *N Engl J Med*. 2021;384(5):403–416.
5. Vallianou NG, Tsilingiris D, Christodoulatos GS, Karampela I, Dalamaga M. Anti-viral treatment for SARS-CoV-2 infection: A race against time amidst the ongoing pandemic. *Metabol Open*. 2021;10:100096.
6. Barda N, Dagan N, Ben-Shlomo Y, Kepten E, Waxman J, Ohana R, et al. Safety of the BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Setting. *N Engl J Med*. 2021 16;385(12):1078–1090.
7. Choi A, Ibañez LI, Strohmeier S, Krammer F, García-Sastre A, Schotsaert M. Non-sterilizing, Infection-Permissive Vaccination with Inactivated Influenza Virus Vaccine Reshapes Subsequent Virus Infection-Induced Protective Heterosubtypic Immunity from Cellular to Humoral Cross-Reactive Immune Responses. *Front Immunol*. 2020 9;11:1166. Doi: 10.3389/fimmu.2020.01166.
8. Misu T, Kortepeter CM, Muñoz MA, Wu E, Dal Pan GJ. An Evaluation of “Drug Ineffective” Postmarketing Reports in Drug Safety Surveillance. *Drugs Real World Outcomes*. 2018;5(2):91–99.
9. Di Fusco M, Moran MM, Cane A, Curcio D, Khan F, Malhotra D, et al. Evaluation of COVID-19 vaccine breakthrough infections among immunocompromised patients fully vaccinated with BNT162b2. *J Med Econ*. 2021;24(1):1248–1260.
10. Ul Munamm SA, Nadeem I, Mahdi N, Saqlain M, Rana ZK, Khatana UF, et al. Comparative analysis of mRNA and inactivated COVID-19 vaccines: A study from Faisalabad district of Pakistan. *J R Coll Physicians Edin*. 2022;52(3):240–246.
11. Ben Fredj S, Ghammem R, Zammit N, Maatouk A, Hadded N, Laadhari H, et al. Characteristics of COVID-19 cases with breakthrough infection in the governorate of Sousse, Tunisia: Sihem Ben Fredj *Eur J Public Health*. 2022;32(Suppl 3):451–2.
12. Abbas S, Abbas B, Amir S, Wajahat M. Evaluation of adverse effects with COVID-19 vaccination in Pakistan. *Pak J Med Sci*. 2021;37(7):1959–1964.
13. Cohen KW, Linderman SL, Moodie Z, Czartoski J, Lai L, Mantus G, Norwood C, et al. Longitudinal analysis shows durable and broad immune memory after SARS-CoV-2 infection with persisting antibody responses and memory B and T cells. *Cell Rep Med*. 2021; 2(7):100354. DOI: 10.1016/j.xcrm.2021.100354.
14. Brunelli SM, Sibbel S, Karpinski S, Marlowe G, Walker AG, Giullian J, et al. Comparative Effectiveness of mRNA-based BNT162b2 Vaccine versus Adenovirus Vector-Based Ad26.COV2. S Vaccine for the Prevention of COVID-19 among Dialysis Patients. *J Am Soc Nephrol*. 2022;33(4):688–697.
15. Galmiche S, Luong Nguyen LB, Tartour E, de Lamballerie X, Wittkop L, Loubet P, et al. Immunological and clinical efficacy of COVID-19 vaccines in immunocompromised populations: a systematic review. *Clin Microbiol Infect*. 2022;28(2):163–177.
16. Mahase E. Covid-19: Vaccinated people are less likely to get long covid, review finds. *BMJ*. 2022;16:376.