

COVID-19 breakthrough infection among vaccinated individuals: A cross-sectional study



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ABSTRACT

Background: A cross-sectional study was carried out in urban area. The primary outcome of the study was the proportion of breakthrough infection in vaccinated subjects, which was defined as any COVID-19 infection occurring ≥ 30 days after receiving both the doses of either of the vaccine(s). **Aims and Objectives:** The aims of this study were to determine prevalence of COVID-19 breakthrough infection among COVID 19 vaccinated patients, (1) to study demographic factors affecting breakthrough infection and (2) to compare the proportion of breakthrough infection among Covishield and Covaxin recipients. **Materials and Methods:** The subjects were selected by systematic random sample method from available vaccination record. A questionnaire was administered in local language containing demographic information and COVID-related information. Nasopharyngeal swab was taken by trained Interns with all necessary precautions, RT-PCR swab was labeled and sent to PCR laboratory in cold chain for testing. **Results:** A total 445 subjects were tested for COVID-19. Subjects included 290 (65.2%) males and 155 (34.8%) females. Maximum cases were from age group of 21–30 year (23.4%). The mean age was found to be 43 year. About 8.85% subjects test result came positive despite taking two doses of either COVID vaccine. Breakthrough infection was more among males than females. Covaxin recipient subjects showed marginally higher percentage of breakthrough infection (9.1%) than Covishield. Out of the 39 breakthrough infections, 16 subjects were having comorbidities. Maximum breakthrough infection was seen in subjects having diabetes mellitus and hypertension both and hypertension alone (1.6%). **Conclusion:** A prevalence of 8.8% of COVID-19 breakthrough infection was reported in our study among fully vaccinated subjects after 30 days of last vaccine dose. Males are at higher risk of getting infection. People with comorbidities are at higher risk of breakthrough infection and hospitalization.

Key words: Breakthrough infection; Comorbidities; COVID-10 vaccine; COVID-19

INTRODUCTION

The mRNA coronavirus disease 2019 (COVID-19) vaccines, Covaxin/Covishield, were 94–95% effective in preventing symptomatic COVID-19 in phase III studies, showing similar efficacy in different age groups, including persons older than 75 years, and persons with comorbidities.^{1,2} In India, 4,25,54,416 discharged COVID-19 cases and 5,24,024 deaths were reported due to COVID-19 by the end of April 2022.³ The Indian vaccination campaign began on 16 January 2021 and relied exclusively on Covaxin and Covishield vaccine. By August 30, 2021, 100,46,40,761 had

received first dose of COVID vaccination, and 89,54,54,221 beneficiaries received second dose of COVID vaccination in India by April 2022 end.⁴ The vaccine effectiveness for the prevention of hospitalization due to COVID-19 was found to be 87% after the second dose in an early case–control study,^{5,6} and 96% in a later comparison of person-time incidence rates from a national registry.⁷ At present, reports from other countries include a US study showing 94% effectiveness after two doses of any mRNA vaccine,^{8,9} and two UK studies that measured an 80–91% effectiveness for prevention of hospitalization of a single dose of BNT162b2.^{10,11}

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Data are lacking on the nature of breakthrough infections with COVID-19 vaccines. No data were published on the clinical characteristics and serological correlates of protection of the study participants who were hospitalized with COVID-19 after vaccination. Immunocompromised individuals were not included in those pivotal studies.

The reproduction rate of COVID infection in India has dropped below 1 implying that 100 infected people are spreading the infection to less than 100 people, to 89 people as the R-value at present stands at 0.89. The COVID-19 situation in the country is improving with the active cases declined to around 3.6 lakh, the lowest in 150 days. However, the country is witnessing a considerable number of breakthrough infections and a very high proportion of the Delta variant is responsible for breakthrough infection after either one of two doses of vaccination according to the Indian SARS-CoV2 Genomics Consortium (INSACOG).^{12,13}

As of July 6, the Centers for Disease Control and Prevention in the United States had received reports of 5,186 patients with COVID-19 vaccine breakthrough infection who were hospitalized or had died. By that day, more than 157 million people in the US had been fully vaccinated, making the breakthrough rate for severe disease a minuscule 0.003 per cent.^{14,15} Such large scale data are not available in India leading to huge gap in knowledge about breakthrough infections in community. Using a sample of vaccinated patients, we aimed to characterize vaccinated patients with breakthrough COVID-19.

Aims and objectives

To determine prevalence of COVID-19 breakthrough infection among COVID 19 vaccinated patients, to study demographic factors affecting breakthrough infection, and to compare the proportion of breakthrough infection among COVISHIELD and COVAXIN recipients.

MATERIALS AND METHODS

A cross-sectional study was carried out in urban area. The primary outcome of the study was the proportion of breakthrough infection in vaccinated subjects, which was defined as any COVID-19 infection occurring ≥ 30 days after receiving both the doses of either of the vaccine(s). The independent variables included age, sex, education, occupation, type of vaccine, and hospitalization.

Sample Size Calculation

The sample size was calculated considering the prevalence of breakthrough infection among general population as 50% as no specific prevalence is available at 95% confidence level, 4% precision, and 10% non-response. The sample size was estimated as 445.

The subjects were selected by systematic random sample method from available vaccination record. The subjects were contacted through telephone, study objective was explained to them and subjects were invited to urban health center.

Ethical clearance

At Urban Health Training Center written informed consent was taken from each individual after explaining the study purpose and procedure. Ethical clearance was taken from the Institutional Ethical Committee (letter number GMCD/IEC/Comm.med/08/2021, dated 25/08/2021). A questionnaire was administered in local language containing demographic information and COVID-related information. Nasopharyngeal swab was taken by trained Interns with all necessary precautions, RT-PCR swab was labeled and sent to PCR laboratory in cold chain for testing. Test results were communicated to subjects. If RT-PCR test is found positive for COVID-19, necessary action such as to quarantine the patient and appropriate treatment for the same was advised. SPSS version 22 was used for statistical analysis using proportion, central tendencies, and Chi-square test to find significance. Chi-square < 0.05 was considered significant at 95% confidence interval.

RESULTS

A total 445 subjects were contacted and tested for COVID-19. Subjects included 290 (65.2%) males and 155 (34.8%) females. Maximum cases were from age group of 21–30 year (23.4%) followed by 41–50 year (19.1%) and 51–60 year (18.2%) (Table 1). The mean age was found to be 43 year (SD = 16.27 variance = 265).

Maximum cases were from Hindu religion 385 (86.5%). About 90% subjects were educated with most of the subjects studied up to HSC (27.4%) followed by graduation (21.3%). About 10.3% subjects were illiterate. About 28.3% subjects were in involved in sales followed by professionals (19.6%).

Out of 445 subjects, 24 subjects showed some form of comorbidities. The distribution of subjects showed that combine diabetes mellitus and hypertension were most common followed by only hypertension.

Figure 1 shows that 80.25% subjects received Covishield vaccine while 18.95 subjects received Covaxin as a preventive measure against COVID-19 disease.

Figure 2 shows RT-PCR rest results for the all 445 subjects. About 8.85% subjects test result came positive despite taking two doses of either COVID vaccine.

Table 2 shows distribution of COVID-positive cases in different age group. Maximum positive cases were seen in 61–70 year age group (1.8%), followed by 51–60 year (1.6%). No significant association was

seen between age group and COVID-19 breakthrough infection.

Table 3 shows distribution of breakthrough infection among males and females. About 51% male and 48.7% females came COVID-positive. Breakthrough infection rate was more among males than females (Chi-square=3.631, P=0.04).

Table 4 shows distribution of breakthrough infection among Covaxin and Covishield recipient. Covaxin recipient subjects showed marginally higher percentage of breakthrough infection (9.1%) than Covishield. No significant association was seen in type of vaccine and breakthrough infection (Chi-square=0.015 P=0.521).

Out of 445 subjects, 24 had one or more comorbidities. Out of the 39 breakthrough infections, 16 subjects were having comorbidities. Maximum breakthrough infection was seen in subjects having diabetes mellitus and hypertension both and hypertension alone (1.6%). Higher chances of breakthrough infection were seen in subjects suffering from comorbidities (Chi-square=153.61, P=0.000). (Table 5) (Figure 3)

Table 6 shows distribution of hospitalization required in breakthrough infection. Around 92.3% of breakthrough infection required hospitalization. Higher chances of hospitalization were seen among breakthrough infection (Chi-square=2.7534, P=0.000).

Table 1: Demographic information of subjects		
	N	%
Age Group		
11–20	23	5.2
21–30	104	23.4
31–40	70	15.7
41–50	85	19.1
51–60	81	18.2
61–70	67	15.1
71–80	13	2.9
81–90	2	0.4
Total	445	100.0
Sex		
Male	290	65.2
Female	155	34.8
Total	445	100.0
Religion		
Buddhist	1	0.22
Hindu	385	86.5
Muslim	58	13.0
Other	1	0.2
Total	445	100.0
Education		
Diploma	13	2.9
Graduate	95	21.3
HSC	122	27.4
Illiterate	46	10.3
Primary	93	20.9
SSC	76	17.1
Total	445	100.0
Occupation		
Agriculture	54	12.1
Clerical	7	1.6
Craft	23	5.2
Professional	87	19.6
Sales	126	28.3
Student	60	13.5
Technician	13	2.9
Unemployed	75	16.9
Total	445	100.0

DISCUSSION

Four hundred and forty-five subjects which have completed two doses of either Covaxin or Covishield were enrolled in the study, to find out prevalence of COVID-19 breakthrough infection. Both the vaccine showed 91.2% protection in preventing the disease, while

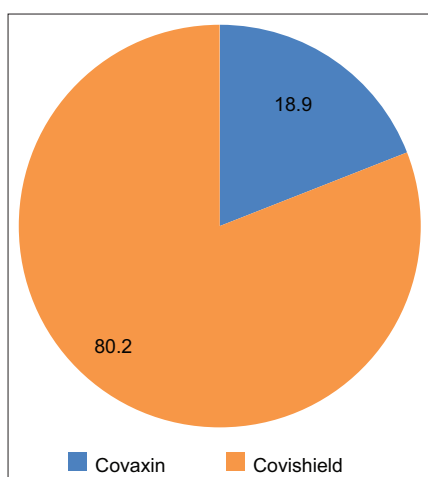


Figure 1: Vaccine received by subjects

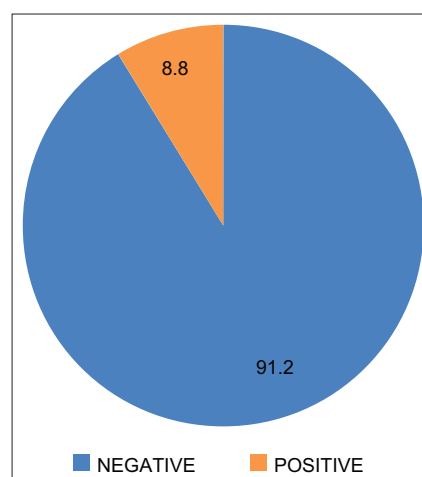


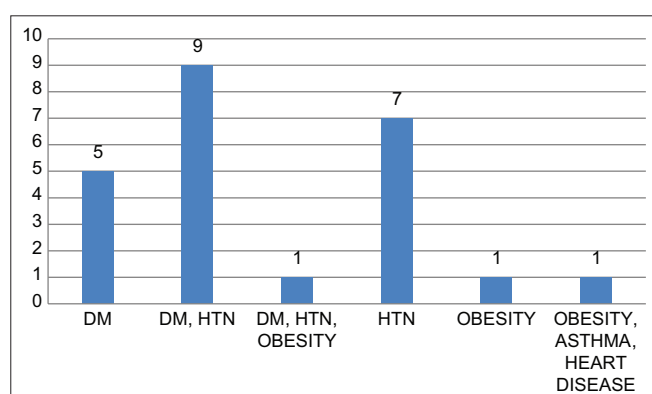
Figure 2: RT-PCR test results for subjects

Table 2: Association between COVID breakthrough infection and Age group of subjects.

RT-PCR result distribution against age group						
	Negative	Positive	Total	Chi-square value	DF	P value
11–20	19	4	23	11.319	7	0.124
	4.3%	0.9%	5.2%			
21–30	95	9	104			
	21.3%	2.0%	23.4%			
31–40	68	2	70			
	15.3%	0.4%	15.7%			
41–50	79	6	85			
	17.8%	1.3%	19.1%			
51–60	74	7	81			
	16.6%	1.6%	18.2%			
61–70	59	8	67			
	13.3%	1.8%	15.1%			
71–80	11	2	13			
	2.5%	0.4%	2.9%			
81–90	1	1	2			
	0.2%	0.2%	0.4%			
TOTAL	406	39	445			
	91.2%	8.8%	100.0%			

Table 3: Association between COVID breakthrough infection and gender of subjects

Breakthrough infection					
	Negative	Positive	Chi-square value	DF	P value
Male	270	20	3.631	1	0.04
	66.5%	51.3%			
Female	136	19			
	33.5%	48.7%			
Total	406	39			
	100.0%	100.0%			

**Figure 3: Comorbidities among subjects**

prevalence of breakthrough infection was 8.8%. A study by Sharma et al.,¹⁶ in healthcare workers, indicate higher prevalence of breakthrough infection 11.3%.¹⁰ Although the population was different as health care workers are more exposed to infected individuals, there was not much difference in the prevalence. Arora et al., in her study also reported prevalence of breakthrough infection as 7.91%.¹⁷ Furthermore, similar to our study, the prevalence

was higher among males than females. The rationale behind it can be associated with several factors including physiological, genetic, and behavioral.

No significant association was seen in type of vaccine used and occurrence of breakthrough infection. (Chi-square=0.015, P=0.521). This suggest both the vaccines are equally effective and other factors play major role in contracting COVID-19 breakthrough infection. In a study by Suri et al., they compared in-hospital outcomes between patients who had received the Covishield (n=181) or Covaxin vaccines. The in-hospital mortality did not differ between the recipients of Covishield or Covaxin in either the fully vaccinated (2 deaths [11.8%] vs. 0 deaths [0%], respectively, P=0.08) or the partially vaccinated cohorts (31 deaths [20%] vs. 28 deaths [17.9%], respectively, P=0.65).¹⁸ The hospitalization rate for breakthrough infection was much higher (92%), but comorbidity was also higher among breakthrough patients. Out of 39 breakthrough case, 16 were suffering from comorbidities such as diabetes mellitus, hypertension, obesity, and COPD. Comorbidities can be the reason behind higher hospitalization among breakthrough cases; in our study, a significant relation was seen in breakthrough infection with comorbidity and hospitalization (Chi-square=2.7534, P=0.000). A study by Sun et al., conducted a cohort study and found that full vaccination was associated with reduced risk of COVID-19 breakthrough infection, regardless of the immune status of patients. Despite full vaccination, persons with immune dysfunction had substantially higher risk for COVID-19 breakthrough infection than those without such a condition.¹⁹ So for persons with immune dysfunction and comorbidities, continued use of non-pharmaceutical interventions (e.g, mask wearing) and alternative vaccine

Table 4: Association between COVID breakthrough infection and vaccine received by subjects

Breakthrough infection in different vaccine						
	Negative	Positive	Total	Chi-square value	DF	P value
Covaxin	80	8	88	0.015	1	0.521
	90.9%	9.1%	100.0%			
Covishield	326	31	357			
	91.3%	8.7%	100.0%			

Table 5 : Association between COVID breakthrough infection and comorbidities among subjects

Breakthrough infection and comorbidities						
	Negative	Positive	Total	Chi-square value	DF	P value
DM	5	0	5	153.61	6	0.00
	1.1%	0.0%	1.1%			
DM, HTN	2	7	9			
	0.4%	1.6%	2.0%			
DM, HTN, Obesity	0	1	1			
	0.0%	0.2%	0.2%			
HTN	0	7	7			
	0.0%	1.6%	1.6%			
No Comorbidities	398	23	421			
	89.4%	5.2%	94.6%			
Obesity	1	0	1			
	0.2%	0.0%	0.2%			
Obesity, Asthma, Heart Disease	0	1	1			
	0.0%	0.2%	0.2%			
Total	406	39	445			
	91.2%	8.8%	100.0%			

Table 6: Association between COVID breakthrough infection and hospitalization required

Hospitalization among breakthrough infection						
	No	Yes	Total	Chi-square value	DF	P value
Negative	391	15	406	2.7534	1	0.00
	96.3%	3.7%	100.0%			
Positive	3	36	39			
	7.7%	92.3%	100.0%			
Total	394	51	445			
	88.5%	11.5%	100.0%			

strategies (e.g., additional doses or immunogenicity testing) are recommended even after full vaccination.

Limitations of the study

The number of documented COVID-19 vaccination breakthrough cases may be significantly underestimated of all SARS-CoV-2 infections among fully vaccinated persons; second, these data are based on passive and voluntary reporting of individuals and might not be a complete representation of breakthrough cases as most of the individuals being asymptomatic or with mild illness post-vaccination might have not got tested; and finally, sequencing of the samples was not conducted, which could have identified the virus lineage that had caused

these breakthrough cases. It is anticipated that even with the administration of effective authorized vaccines, breakthrough cases are expected to happen, until the immunity reaches sufficient levels among the population to further decrease transmission.

CONCLUSION

The current study concludes that a prevalence of 8.8% of COVID-19 breakthrough infection was reported in our study among fully vaccinated subjects after 30 days of last vaccine dose. Males are at higher risk of getting infection. People with presence of comorbidities are found to be at higher risk of breakthrough infection and hospitalization due to impaired immunity. In such cases the use of non-pharmaceutical interventions (e.g., mask wearing and safe distancing) is recommended to avoid transmission of infection in them.

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