

Original Article

A study on Breakthrough Infections of COVID-19 from an Urban Healthcare Centre in Kerala

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Background and Aim : While India's vaccination drive against COVID-19 continues to progress, the number of Breakthrough Infections are also revealing an uptick due to Community spread of COVID-19. There is a dearth of data quantifying the extent of breakthrough infections, defined as infections following two doses of vaccine. We aimed to understand the occurrence of Breakthrough Infections among the public in the City of Thrissur, Kerala, India, during the recent surge of COVID-19 in Kerala.

Methods : Patients visiting the Internal Medicine Outpatient Department (OPD) in a private hospital in the City of Thrissur in Kerala, India were selected for the study. Subjects above the age of 18 years presenting to the OPD between August 01, 2021 and September 30, 2021 were surveyed through a short interview on the COVID-19 infection history, symptoms, severity and vaccination status.

Results : Of the 56 participants who tested positive for COVID-19, 38 had received both doses of vaccine and all had received their first dose of vaccine. 4 patients had no symptoms, 37 patients reported mild symptoms and nine patients reported moderate to severe symptoms.

Conclusion : Our study demonstrates the occurrence and describes the epidemiology of COVID-19 breakthrough infections in a City from the Indian State of Kerala in a real-world setting. We conclude the occurrence of Symptomatic Breakthrough Infections of COVID-19 in patients who had received two doses of the vaccine were mild in the majority of the patients (87%). Further research is required to understand the mechanisms behind these Breakthrough infections.

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Key words : COVID-19, Breakthrough infections, Coronavirus.

Coronavirus disease 2019 (COVID-19) has taken a toll globally since its emergence in 2019. With millions of people being infected with a rising death toll world wide, the race for a vaccine could not have been any faster. Many pharmaceutical companies developed vaccines aiming to reduce hospitalization and mortality rates associated with COVID-19. A country highly affected by this virus is India, with over 450,000 deaths. In India, two vaccines were developed targeting this virus: ChAdOx1 nCoV-19 and Covaxin/BBV152. Both vaccines require two doses. Covishield uses a weak version of the adenovirus, while Covaxin

Editor's Comment :

- Our study from an urban community setting, reveals that breakthrough infections do occur in vaccinated individuals. However, the severity of disease is less intense. With proper physical distancing measures and use of personal protective equipment, we can reduce the community burden of COVID-19.

uses an inactivated SARS-CoV-2 virus¹⁻³.

Vaccine Breakthrough Infections are defined as the detection of SARS-CoV-2 RNA or antigen in a respiratory specimen collected from a person ≥ 14 days after they have completed all recommended doses of an approved COVID 19 vaccine^{4,5}. These Breakthrough Infections need to be understood better; however, accurate data from real world settings are very few⁶. Vaccines are effective in decreasing the risk of being infected with COVID-19 by 70-90% and also prevent severe infections⁷⁻⁹. These infections could occur due to the COVID-19 variants which may bypass vaccine-induced immunity⁷. A rising number of cases of vaccine Breakthrough Infections are being found in regions with a higher occurrence of COVID-19 cases.

During the months of August and September of

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2021, the State of Kerala in India witnessed a high daily count of COVID-19 cases with over 120,000 cases possibly due to a second wave². We decided to study the real world occurrence of vaccine breakthrough infections in patients presenting to an Outpatient Department (OPD) of a private hospital based in Thrissur, Kerala. In addition, there have been non-scholarly reports regarding Breakthrough Infections questioning the efficacy of the vaccine as the daily number of cases rise.

We investigated COVID-19 Breakthrough Infections in partially and fully vaccinated participants.

MATERIALS AND METHODS

Study Setting and Participants

Patients visiting the Internal Medicine OPD at a private hospital in the city of Thrissur in Kerala, India were selected for the study. The OPD has a footfall of approximately 30 patients daily. Patients visiting the OPD came for routine examinations as well as some urgent care issues. Telemedicine patients and in-person visit patients were also included in the study.

Exclusion criteria : We excluded participants who were less than 18 years of age and those who tested negative for COVID-19 despite showing symptoms. Inclusion criteria: Participants above the age of 18 years presenting to the OPD between August 01, 2021 and September 30, 2021, were enquired through a short interview. A verbal informed consent was obtained from all the patients enrolled into the study, after providing them a written consent form in the local language which participants could read and understand (refer to Appendix A for a copy of the informed consent). For telemedicine patients, informed consent was obtained via text messages.

A medical professional enquired participants regarding their vaccination status and if they tested positive for COVID-19 any time after they received the first or second dose of the COVID-19 vaccine. If they tested positive (using PCR or Rapid Antigen Test), the date of the positive test was recorded along with the month when they received the COVID-19 vaccination. The type of COVID-19 vaccine administered was also recorded. They were further enquired on their symptoms during and after they tested positive for COVID-19 and whether they needed hospitalization. In addition, participants were asked for any residual symptoms. Symptoms were classified as mild (if they were self limiting or only required outpatient treatment), moderate if they required hospitalization but not needing intensive care and severe if ICU(Intensive Care Unit) care was needed. We tabulated the number of patients who were positive for COVID-19 and calculated

the risk of mild, moderate and severe infections. Comorbidities of participants were assessed as well.

Statistical Analysis :

IBM SPSS version 27.0.1.0 was used for data calculation and analysis. Variables measured were age, gender, comorbidities, receipt of first dose of COVID-19 vaccine, receipt of second dose of COVID-19 vaccine, status of COVID-19 infection, hospitalization status due to COVID-19, symptoms of COVID-19 infection and residual symptoms. Missing values were coded as "999" on SPSS. Only COVID-19 positive patients were included in the analysis. We conducted descriptive analysis for demographic and comorbidities and cross-tabulation.

RESULTS

Demographics

There were a total of 56 participants tested positive for COVID-19 (16 males and 40 females). The mean age was 48 years (SD \pm 14 years). All patients (n=56) had received their first dose of the COVID-19 vaccine and 38 patients received the second dose of the vaccine. Most of the patients received COVISHIELD except one patient who had received COVAXIN.

Comorbidities and Symptoms

There were 28 patients with comorbidities.

Comorbidities included Diabetes Mellitus (n=14), Systemic Hypertension (n=11), Thyroid Disease (n=2), Dyslipidemia (n=1), Cardiovascular Disease (n=5), Lung Disease Including Asthma (n=6), Chronic Kidney Disease (n=1), Anemia (n = 1) and Cancer (n= 1).

Symptoms included fever, cough, sore throat, chills, throat pain, vomiting, body pain, dyspnea, delirium, and joint pains. They were categorized as asymptomatic, mild and moderate to severe hence, the exact percentage of participants reporting the type of symptom was not obtained. Moderate to severe symptoms included the requirement for inpatient care through hospitalization or requirement of supplemental oxygen, anticoagulants, steroids, severe cough and breathlessness needing Intensive Care Unit admission.

There were four patients that reported no symptoms, 37 patients reported mild symptoms and nine patients reported moderate to severe symptoms. Three patients were hospitalized. There was no mortality (Fig 1).

Recovery

All participants had recovered well. Recovery ranged from two days to 15 days. Four patients had residual shortness of breath and cough. The remaining patients did not have any residual symptoms. Overall, all patients recovered well.

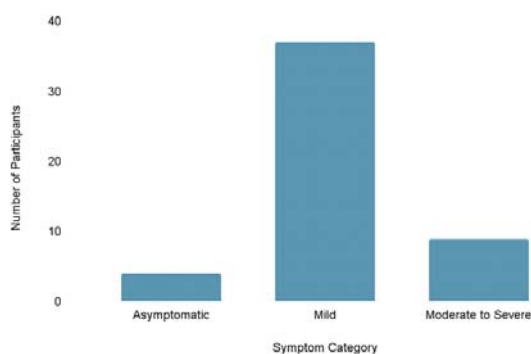


Fig 1 — Number of participants with a COVID-19 positive test and their respective presenting symptoms categories

DISCUSSION

To the best of our knowledge, peer reviewed publications on breakthrough infections from Kerala, the Southern state of India, especially in a community setting, is limited¹⁰⁻¹². In the beginning of April 2021, Indian Healthcare System and population were overwhelmed by COVID-19 cases and mortality due to a new variant B.1.617.2 (Delta) causing the second wave of COVID pandemic¹³. This study is unique in identifying the demographic characters and risk factors of breakthrough infections during the second wave of the COVID-pandemic in the Indian sub-continent.

Data from the Southern State of Kerala is interesting from an epidemiological standpoint since the state has reportedly less COVID-19 associated mortality compared to the rest of India. Also, Kerala reported high vaccine uptake very early during the roll out of India's vaccination campaign. However widespread community spread in an aging population living in highly dense communities might have caused breakthrough infections in susceptible populations. Most reported data on vaccine breakthrough infections are from North America and Europe and hence it is important to understand our study results highlighting the epidemiology of breakthrough infections in South India. Although genomic surveillance was not done in our cohort, it is quite possible that variants of concern B.1.617.2 and B.1.1.7 might have been major causative factors for the spread of Breakthrough Infections amongst vaccinated individuals similar to that documented in the AIIMS study published from New Delhi, the Capital City of India¹⁴.

We have reported the risk factors and disease profile of Breakthrough Infections in a real-world setting. In an analysis reported by Antonell *et al* in a large cohort of 1.2 million COVID Symptom Study app users, less than 1 percent of the study population reported Breakthrough Infections¹⁵. The main risk

factors characterized were frailty, age ≥ 60 years, residing in highly deprived areas and higher BMI. Vaccination was associated with reduced odds of hospitalization or having more symptoms in the first week of illness following the first or second dose, and long-duration (≥ 28 days) of symptoms following the second dose. Similarly, among those patients with Breakthrough infections due to delta variant requiring hospitalization ($n=126$) as reported by Bosch *et al* based on data from the state of Florida, risk factors identified were age, immunocompromised status and presence of comorbidities such as Diabetes, Chronic Kidney Disease, Coronary Artery Disease and Hypertension¹⁶. Data reported from Chile by Duarte *et al* reflect similar findings¹⁷. In this study of 38 breakthrough cases, only two patients developed moderate-severe disease. Both cases were adults over 60 years old and had comorbidities. A study on breakthrough infections among Healthcare Workers in Kerala was reported by Niyas *et al*¹⁸. All cases were mild because the affected individuals were younger (mean age 32 years), mostly women (67%) and did not have that many risk factors for severe disease. Among the 108 reported cases, there was no hospitalization or mortality. Comorbidities such as Diabetes, Hypertension, Malignancy and Chronic Lung Disease were present only in seven patients. Breakthrough infections occurred after two months of vaccination (mean = 69 days).

Dash *et al* has reported data from the State of Orissa, India but noted a 10 percent risk of hospitalization in those with Breakthrough Infections¹⁹. Age was identified as the main risk factor in this study. In the Desai *et al* study reporting the epidemiology of breakthrough infections among employees of the All India Institute of Medical Sciences (AIIMS), a Tertiary Care Hospital in New Delhi, India in the context of a huge surge in cases, the vaccine effectiveness of BBV152 was found to be only 50% (95% CI 33–62) against symptomatic laboratory-confirmed COVID-19²⁰. It is interesting that our cohort did not demonstrate a higher rate of symptomatic infections despite having a higher age demographic. This must have been partly due to the strict adherence to public health measures, higher literacy rates and better socio-economic status among the people of Kerala. In another cohort reported from Delhi, India among healthcare workers (HCWs) by Sharma *et al*, 325 HCWs with a mean age of 29 years, predominantly men, had a 13% incidence of breakthrough infections²¹. Most Breakthrough Infections were mild without hypoxia or requirement of hospitalization. This is

possibly due to the younger age group of the study participants. Genomic surveillance of Breakthrough Infections from Kerala was reported by Philomina *et al* in a cohort of six patients²². Four patients were diagnosed with the B.1.1.7 variant of SARS-CoV-2 in the above study. A study from West Bengal, where a higher incidence of deaths among Health Care Workers (HCW) were reported even after months of rolling out vaccines revealed that about 37% HCW were hesitant to take the vaccines²³. Our study clearly depicts that despite the rise in breakthrough infections, number of deaths or serious illness due to COVID-19 is negligible among the fully vaccinated individuals. Thus our study aids to address the vaccine hesitancy among the HCW and population at large and stresses the importance of complying with the required doses of COVID vaccines.

Limitations

Limitations of our study include the small sample size, sample selection only from an outpatient setting, lack of comparison data from the rest of the state, lack of data on exposure setting, socio-economic status, substance use, SARS CoV-2 gene sequencing and antibody titres (5, 24-26). Genetic sequencing is important as reported by Christensen *et al*/based on breakthrough infections analyzed in Houston²⁵. This group was able to confirm that the Delta variant caused a significantly higher rate of vaccine breakthrough cases (23.7% *versus* 6.6%) compared to all other variants combined. This study also documented that fully vaccinated individuals can transmit SARS-CoV-2 to others. We also cannot confirm the risk factor profile in individuals who may have received the two doses of the vaccine in a different dose interval schedule or in those who received mRNA based vaccines or mixed immunization. The main highlight of our study is that this data will be an important addition to the literature on COVID Vaccine Breakthrough Infections from various parts of India under diverse clinical and community settings. Our results are strengthened by the true documentation of asymptomatic and symptomatic infections through PCR testing.

Prospective Research

More research is needed about the Epidemiology of Breakthrough Infections in the setting of emerging variants. A recent study by Shenoy *et al*/demonstrated that those with hybrid immunity may have the best protection against re-infections. This needs to be studied further in the light of waning immunity and spread of newer variants²⁷. Also we need to understand the potential incidence or absence of long-COVID syndromes in those with Breakthrough Infections and

reinfections. A further follow up of these patients for a longer period of time can shed light on the continued protection against emerging variants owing to their hybrid immunity against the COVID-19 virus.

Conclusion :

In conclusion, Breakthrough Infections are a major concern in India. Results from this study support the need for further investigation on the reasons behind breakthrough infections including protective mechanisms. Our research adds to the emerging literature of Breakthrough Infections and sheds light for future research. Our study demonstrates the occurrence and describes the epidemiology of COVID-19 breakthrough infections from an urban centre in the state of Kerala in a real-world setting. We reported mild symptomatic Breakthroughs of Cases of patients who have been affected with COVID-19 after taking the vaccination either first dose or both. Further research is required to understand the mechanisms behind these Breakthrough Infections. Also we need to follow such patients to understand if they get continued protection against emerging variants owing to their hybrid immunity against the COVID-19 virus. To minimize SARS-CoV-2 infection, at-risk populations must be targeted in efforts to boost vaccine effectiveness and infection control measures. Our findings might support caution around relaxing physical distancing and other personal protective measures in the postvaccination era, particularly around frail older adults and individuals living in more deprived conditions.

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