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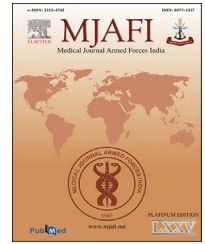
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## Original Article

# Epidemiological analysis of SARS-COV-2 B.1.617.2 (delta variant) transmission in an educational institute

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## ABSTRACT

**Background:** Despite having an effective COVID-19 vaccine, the COVID-19 pandemic is far from over and the delta variant continues to cause havoc across several continents. The present study was conducted to analyze and describe the occurrence of COVID-19 cases among completely vaccinated individuals.

**Methods:** In an educational institute in Western Maharashtra, we analyzed a cluster of RTPCR positive COVID-19 cases among fully vaccinated students which occurred in 12 days. The cases were linked to a series of curricular and co-curricular events in the institute. A detailed epidemiological investigation and genome sequencing of cases were conducted. IgG antibodies against S1 protein of novel SARS-CoV-2 were estimated for cases and age, sex, and vaccination status matched controls.

**Results:** All 37 identified cases were mild COVID. 188 high risk (HR) contacts of the cases were identified. The overall secondary attack was 9.5%. Out of 31 cases and 50 controls, 09 (29%) cases and 08 (16%) controls were found to have IgG antibodies against S1 protein of novel SARS-CoV-2 titer of more than 60 U/ml. Whole-genome sequencing of 15 samples of the cluster showed the presence of the Delta variant of SARS-CoV-2. No correlation was observed between Ct value and IgG S1 antibody titers.

**Conclusion:** The study provides significant evidence that only vaccination alone does not completely protect against SARS-CoV-2 B.1.617.2 (Delta) variant infection. An all-encompassing multicomponent strategy involving implementation of NPIs, robust

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contact tracing, early identification and isolation of cases, and high vaccination coverage is the way forward for the prevention of COVID-19.

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## Introduction

COVID-19 was declared a pandemic by WHO on 11 March 2020.<sup>1</sup> The disease has wreaked havoc in more than 180 countries across the globe.<sup>2</sup> As of August 2021, the world has witnessed a total of 217,558,771 COVID-19 confirmed cases and 4517240 deaths.<sup>2</sup> India, being one of the worst affected countries in the pandemic, has reported 328,10,845 cases and 439020 deaths as of Aug 2021.<sup>3</sup> In India, the deadly second wave can be attributed to the Delta variant (B.1.617.2) which was first identified in October 2020, in Maharashtra. India started vaccination against COVID-19 in Jan 2021 and by Aug 2021 it had vaccinated more than 35% of the population.<sup>4</sup> The emergence of Delta variant in India, its rapid spread across the globe and reports of decreased vaccine effectiveness against the Delta variant has been a matter of concern for governments and scientific communities. In a study conducted by Lopez et al. the effectiveness after one dose of either BNT162b2 or ChAdOx1 nCoV-19 vaccine was notably lower against the Delta variant than the alpha variant.<sup>5</sup>

In the recent past there have been a series of reports of mass gatherings driving up the number of cases and even causing focal outbreaks. One such event was the Kumbh Mela gathering in India which resulted in large clustering of cases.<sup>6</sup> A similar study from Massachusetts reported occurrence of 469 cases, associated with a mass gathering and among which more than 70% were break through infections.<sup>7</sup>

In a closed community of highly vaccinated population, the phenomenon of Super Spreader Events can drive a sudden rise in cases. A super-spreader, usually identified in retrospect, has a greater than average propensity to infect a larger number of people in a setting or events which facilitates higher transmission.<sup>8</sup> The present study was conducted to analyze occurrence of COVID-19 cases in completely vaccinated individuals in a teaching institute.

After the first wave of the pandemic in the country, educational institutions and workplaces have adopted various strategies to prevent COVID-19 after reopening. Various agencies have given guidelines for prevention of COVID-19 in educational institutes.<sup>9,10</sup> Recommended preventive strategies primarily aimed to prevent occurrence of a case of COVID-19 are use of face mask, social distancing and hand hygiene. The secondary preventive measures include early testing of symptomatic individuals followed by identification of contacts and their testing, quarantine, and isolation.

## Materials and methods

It was a longitudinal follow-up study conducted among vaccinated medical students. The details of study setting, and

other factors taken into consideration to describe and analyze occurrence of COVID-19 cases in the campus are provided in the following paragraphs. The study was approved by the institutional ethics committee.

### Study setting

This study analyses the transmission dynamics of a cluster of COVID-19 cases, which occurred in August 2021 among students at a Medical College in western Maharashtra. The institute has more than 500 students studying in four batches in various academic years. It is mandatory for all students to stay inside the campus. At the time of the occurrence of COVID-19 cases in campus students from all four batches, that is, first year to fourth year were present in the college.

Boys and girls reside in separate hostels; however, they share a common dining place. The students hostel consists of three types of rooms—double-occupancy rooms, single-occupancy rooms, and single-occupancy rooms with balcony. All floors have common bathrooms and toilets. Students from each academic year attend lectures, practical sessions and clinics in various strengths. Most of the students are actively involved in various co-curricular and extracurricular activities. All the students were fully vaccinated with two doses of COVISHIELD vaccine (for all the students at least 3 months had passed since the inoculation of the second dose of vaccine).

### Timeline of events

Inescapable student-related activities were organized with effect from 31 July till 04 August. These activities were a mix of outdoor and indoor events with due COVID-19 precautions. On 31 July 21, a cultural event was organized in the college auditorium, which was attended by more than 450 students. Use of mask was compulsory for attending the events. The duration of the event was 3 h. No pretesting or screening was mandatory for attending the events. Subsequently, in next few days a number of outdoor and indoor sports/cultural events were also conducted. Owing to human behavior heterogeneity, few breaches of COVID-appropriate behavior apparently happened during the various events. An individual with influenza-like illness (ILI) tested positive for COVID-19 on 03 August 21. Further occurrence of the cases among students have been depicted in Fig. 1.

### Testing policy

The students undergo investigations and treatment for various illnesses in the campus Medical Inspection (MI) Room. All symptomatic individuals with ILI-like symptoms are tested with COVID-19 reverse transcriptase polymerase chain reaction (RT-PCR).

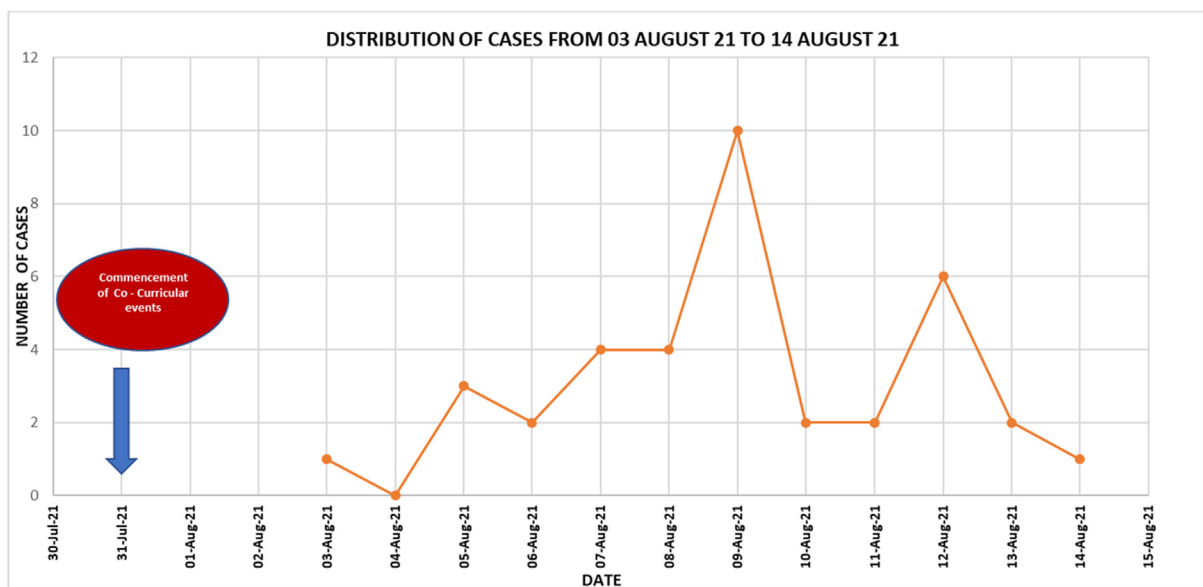


Fig. 1 – Date-wise distribution of cases.

#### Epidemiological investigation and preventive action

All students were been regularly sensitized regarding the signs and symptoms of COVID-19, on development of any sign or symptom the students reported to doctor on campus and were tested for COVID-19 by RT-PCR. All symptomatic students were kept in isolation till RT-PCR reports were available, all positive cases were isolated in single rooms in a separate building. A case is defined as any individual with a positive COVID-19 RT-PCR test. On occurrence of a case, the designated contact tracing team of the institution carried out detailed contact tracing of case. Individuals who were floor mates of the case and individuals with any specific contact of with case were considered as high-risk contacts. Details of contacts from same batch and other social contacts of the case were also recorded as part of history taking. Complete travel history, vaccination history, previous history of COVID-19, history of attending training activities, extracurricular activities, and any social gathering was recorded for all cases. History on clinical aspects including symptomatology, severity of disease, hospital admission/home isolation, and treatment received were also collected during follow-up of cases. All the high-risk contacts were screened in the MI room for symptoms. Only symptomatic contacts were tested.

#### Serum anti-S1 IgG antibody estimation

After obtaining informed written consent 5 ml of peripheral blood was collected under aseptic precautions from 31 cases and 50 controls matched for age, sex, and vaccination status. Serum was separated within an hour of sample collection and stored in 2 ml of cryovial at  $-20^{\circ}\text{C}$ . Quantitative estimation of IgG antibodies in serum samples against S1 protein of novel SARS-CoV-2 was performed using EDITM (Epitope Diagnostics, Inc, USA, a quantitatively SARS-CoV-2 enzyme-linked immune-sorbent assay (ELISA)-based kit in a 96-well micro-titer plate). The antibody levels were expressed as U/ml

and a value of over 60 U/ml was considered protective as per the recommended cut-off provided by the manufacturer.

#### SARS-CoV-2 whole-genome sequencing

SARS-CoV-2 RT-PCR positive cases with cycle threshold (Ct) values for envelope (E) gene target of 25 or less were selected for whole genome sequencing, that is, a total of 18 samples were processed for gene sequencing. Briefly, RNA extraction from stored viral transport medium at  $-70^{\circ}\text{C}$  was performed using Qiagen (Germany) RNA extraction kit. Library preparation and sequencing by  $2 \times 250$  bp chemistry was performed on Illumina MiSeq platform using prior established protocol.<sup>11</sup> Phylogenetic analysis and functional evaluation of variants was performed by neighbor-joining method, with 1000 bootstrap replications.

## Results

On 3<sup>rd</sup> August 2021, one student was detected to be SARS-CoV-2 positive by RT-PCR. The student had mild symptoms, was completely vaccinated, and did not have history of previous COVID-19 infection. Thereafter, between 03 and 14 August 2021, out of 450 students of the first, second, and third academic years, 37 tested SARS-CoV-2 positive. The timelines of occurrence of cases have been depicted in Fig. 1. Baseline characteristics of the cases have been described in Table 1. Majority of the cases were males - 32 (86.4%) and mean age of the cases were 23 years. However, there were no cases from the final year batch. All the cases had completed second dose of vaccination by the end of March 2021 and had no h/o previous laboratory-documented SARS-CoV-2 infection. All cases were mild COVID-19, with only 3 among 37 cases hospitalized for monitoring as they were detected to have concomitant dengue infection during the period of isolation. No cases required oxygen support or assisted ventilation.

**Table 1 – Baseline characteristics of cases.**

	Cases (%) (n = 37)
Sex	
Male	32 (86.4)
Female	5 (1.35)
Age	
mean ±SD	20.3 (±0.94)
Academic year	
First year	13 (35.1)
Second year	16 (43.2)
Third year	08 (21.6)
Fourth year	00 (00.0)
Type of accommodation	
Single room	24 (64.8)
Double room	6 (16.2)
Single room with balcony	7 (18.9)
Symptoms	
Fever	19 (51.3)
Sore throat	9 (24.3)
Cough	4 (10.8)
Coryza	4 (10.8)
Anosmia	1 (2.7)
Attendance in social gatherings	37 (100)

A thorough epidemiological investigation was carried out for each case. It was observed that all the cases participated in the indoor activities. Eighteen cases were identified as high risk (HR) contacts of cases from the cluster. Five cases were identified to be having contact during practice sessions for the abovementioned activity, which may have aided to the transmission. In addition, social contacts between some cases were also established, which occurred during classes and other activities (Fig. 2). During the contact tracing for the fresh cases a total of 188 HR contacts were identified and the overall secondary attack rate was found to be 9.5% (Table 2). No case

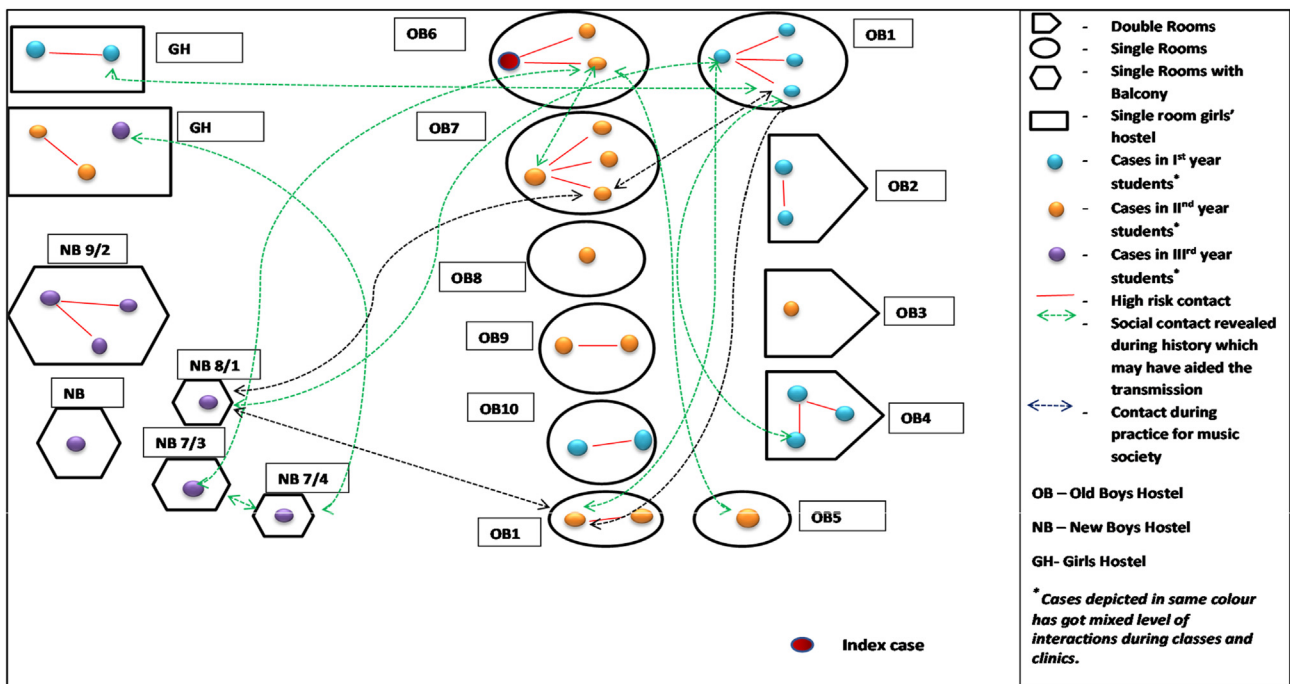
had history of recent travel history to any other districts or state. The mean time interval between onset of symptoms and testing was 1.3 days. The maximum gap was of 4 days and minimum 1 day.

As all the students in the institute are completely vaccinated, to assess the baseline antibody levels, we carried out quantitative estimation of IgG antibodies against S1 protein of novel SARS-CoV-2 for 31 cases (3 cases were unwilling and 3 had co-infection with dengue). Only 9 (29%) and 8 (16%) were found to have more than 60 U/ml of IgG antibodies against S1 protein of novel SARS-CoV-2 (as per recommended cutoff provided by the manufacturer) (Table 3). Fifteen samples of CT value 25 or less were processed for whole-genome sequencing. All the 15 samples were of Delta variant of SARS-CoV-2, out of which 5 samples were found to be of AY.12 sublineage of the Delta variant.

**Discussion**

The study reveals that a multipronged preventive strategy along with high vaccination coverage are critical in limiting the spread of COVID-19 in a residential college setup. The study findings are aided by the unique conditions of the study population—a young fully vaccinated group contained in a small geographical area with limited restriction on curricular or co-curricular training activities albeit with strict implementation of COVID-19 preventive measures, robust contact tracing, early identification, and isolation of cases.

In our study, all the 37 cases were symptomatic, with fever being the predominant symptom. All were mild cases, and only three cases required hospital admission due to co-infection with Dengue virus as a precautionary measure. During hospitalization they remained mild symptomatic and



**Fig. 2 – Distribution of cases and pattern of contact.**

**Table 2 – Secondary attack rate.**

Total high-risk contacts (HRCs) identified	Total HRCs turned positive	Secondary attack rate (%)
188	18	9.5

**Table 3 – Antibody titers of SARS-COV-2 S1 protein.**

	Positive	Negative	Total	p value <sup>a</sup>
Cases	9 (29.0%)	22 (71.0%)	31	0.161
Controls	8 (16.0)	42 (84%)	50	

<sup>a</sup> Chi-square value - 1.9599, df - 1.

did not require supplementary oxygen. All the 37 cases had mild disease due to young age (mean age 23 years), no history of any comorbidity and were completely vaccinated. Several large-scale population-based studies from a number of countries namely, Israel, Spain, United Kingdom etc. as well as from India have shown that complete vaccination protects against severe illness and hospitalization in all age groups.<sup>12–16</sup>

Educational institutes especially those with residential campuses have implemented several measures such as strict compliance to COVID-appropriate behavior, regular screening for symptoms and ensuring maximum coverage of vaccination. In our institute also, all the COVID-19 prevention measures were followed very religiously. We had a distinct advantage of 100% vaccination coverage; hence, only 37 symptomatic cases of COVID-19 occurred out of more than 500 students present in the campus in spite of extra-curricular activities and no restriction on peer interaction. A number of studies have shown occurrence of cases after mass congregations or public gatherings.<sup>17–20</sup> One of the studies with similar settings was reported by Doyle et al,<sup>17</sup> which analyzed an outbreak of 158 cases of COVID-19, among undergraduates returning to university campus after Spring Break, Chicago, Illinois from March to May 21, the median age of cases was 19.4. However, unlike our study only 3% of the cases were fully vaccinated. In another similar case study by Matthias et al<sup>19</sup> in a COVID-19 cluster associated with a church camp for persons aged 14–18 years and a men's conference in Illinois, USA, in June–July 2021 an attack rate of 7% was reported among the camp attendees. The overall percentage of fully vaccinated among cases was less than 50%. Among 31 samples sequenced from the cases more than 85% was of B.1.617.2 or the Delta variant. In our study, all the cases were connected either by virtue of belonging to the same batch or same hostel or social group or having attended the social gatherings, after a thorough epidemiological investigation we found SAR of 9.5% among contacts and 100% samples were B.1.617.2 or the Delta variant. Similarly, in a cluster of 27 cases of COVID-19 among unvaccinated students in an elementary school in California, with more than 50% SAR by one single index case,<sup>18</sup> reported all 18 available samples to have Delta Variant. It is now well established that Delta is the dominant variant circulating in India and many countries across the globe. The low transmission and occurrence of only a few cases in our study can be attributed to strict implementation of multi-component COVID-19 control strategy involving monitoring of adherence to COVID-appropriate behavior by students, robust

contact tracing, early identification and isolation of cases and 100% vaccination coverage. Effectiveness of similar preventive strategy was demonstrated in over 7000 campers and staff members attending overnight camps in the United States.<sup>21</sup>

In our study, we found that there was no significant difference in the presence of IgG antibodies against S1 protein of novel SARS-CoV-2 between cases and controls, which is expected because both the groups were vaccinated with the same vaccine, that is, ChAdOx1 nCoV-19 vaccine (Covishield). Certain studies have indicated that antibody levels decline with the passage of time. In a preprint published by Powel et al<sup>22</sup> it was observed that protection offered by both Pfizer–BioNTech and Oxford–AstraZeneca COVID-19 vaccine waned with passage of time. AstraZeneca's effectiveness fell from 69% to 61% after 90 days of the second dose. With emergence and rapid community spread of highly mutated variants of concern like Omicron, which are proving to have high transmissibility and secondary attack rate among close contacts and a potential for probable immune escape from vaccination immunity the need of non-pharmacological intervention in COVID prevention during gathering remains highly significant.<sup>23</sup>

One of the notable findings of our study is that all the 37 cases, which occurred over a span of 2 weeks were from the first three academic batches and not a single student from the final year batch was affected despite their participation in the extra/co-curricular and training activities as well as sharing the same residential accommodation. Investigation revealed that the final year students were more conscious of rigorously following COVID-appropriate behavior and had reduced social interaction with other batches due to periodic exams and academic engagements. Informal interaction with the final year students revealed that they scrupulously followed COVID appropriate behavior because contracting infection at this stage would entail loss of study time or even not being able to appear for the exams, which may have detrimental effect on their career.

## Conclusion

Our study has the unique distinction of describing an occurrence of COVID-19 cases in fully vaccinated individuals. The study significantly echoes and provides real-life evidence regarding infections due to SARS-CoV-2 B.1.617.2 (Delta) variant. Firstly, COVID-19 vaccination may not provide complete protection against the B.1.617.2 (Delta) variant infection;<sup>19</sup> however, vaccine protects against severe illness and hospitalization. Secondly, having IgG antibodies in serum samples against S1 protein of novel SARS-CoV-2 may not translate to protection against B.1.617.2 (Delta) variant. Lastly and most importantly, strict implementation of non-pharmacological interventions, robust contact tracing, early identification and isolation of cases, and high vaccination coverage should be the guiding principles for all educational institutes.

## Disclosure of competing interest

The authors have none to declare.

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