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First and second doses of Covishield vaccine provided high level of protection against SARS-CoV-2 infection in highly transmissible settings: results from a prospective cohort of participants residing in congregate facilities in India

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ABSTRACT

Objectives This study aimed to determine the effectiveness of Covishield vaccine among residents of congregate residential facilities.

Design A prospective cohort study in congregate residential facilities.

Setting Dharamshala, Himachal Pradesh, India, from December 2020 to July 2021.

Participants Residents of all ages in seven facilities—three monasteries, two old age homes and two learning centres—were enrolled.

Exposures First and second doses of Covishield vaccine against SARS-CoV-2 infection.

Main outcomes measures Primary outcome was development of COVID-19. Secondary outcome was unfavourable outcomes, defined as a composite of shortness of breath, hospitalisation or death. Vaccine effectiveness (%) was calculated as (1−HR)×100.

Results There were 1114 residents (median age 31 years) participating in the study, 82% males. Twenty-eight per cent (n=308/1114) were unvaccinated, 50% (n=554/1114) had received one dose and 23% (n=252/1114) had received two doses of Covishield. The point prevalence of COVID-19 for the facilities ranged from 11% to 57%. Incidence rates (95% CI) of COVID-19 were 76 (63 to 90)/1000 person-months in the unvaccinated, 25 (18 to 35)/1000 person-months in recipients of one dose and 9 (4 to 19)/1000 person-months in recipients of two doses. The effectiveness of first and second doses of Covishield were 71% (adjusted HR (aHR) 0.29; 95% CI 0.18 to 0.46; p<0.001) and 80% (aHR 0.20; 95% CI 0.09 to 0.44; p<0.001), respectively, against SARS-CoV-2 infection and 86% (aHR 0.24; 95% CI 0.07 to 0.82; p=0.023) and 99% (aHR 0.01; 95% CI 0.002 to 0.10; p<0.001), respectively, against unfavourable outcome. The effectiveness was higher after 14 days of receiving the first and second doses, 93% and 98%, respectively. Risk of infection was higher in persons with chronic hepatitis B (aHR 1.78; p=0.034) and previous history of tuberculosis (aHR 1.62; p=0.047).

Conclusion Covishield was effective in preventing SARS-CoV-2 infection and reducing disease severity in highly transmissible settings during the second wave of the pandemic driven by the Delta variant.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Data are limited on how individuals residing in highly transmissible congregate living facilities fared during the deadly second wave of the COVID-19 pandemic in India.

⇒ Data on effectiveness of Covishield vaccine (Oxford-AstraZeneca) including durability of protection against infection and unfavourable outcomes in diverse populations are needed.

⇒ Tibetan refugees residing in monasteries and nunneries constitute a vulnerable population at high risk of COVID-19.

WHAT THIS STUDY ADDS

⇒ Prevalence of COVID-19 in the congregate living facilities ranged from 11% to 57%.

⇒ In following 1114 residents over 3628 person-months, COVID-19 incidence rate was ninefold higher in the unvaccinated than those who received two doses (unvaccinated 76 (95% CI 63 to 90) per 1000 person-months; one-dose recipients: 25 (95% CI 18 to 35) per 1000 person-months; two-dose recipients: 9 (95% CI 4 to 19) per 1000 person-months).

⇒ After 2 weeks of vaccine administration, effectiveness >90% against SARS-CoV-2 infection and unfavourable outcomes was observed for the first and second doses of Covishield.

⇒ Residents who had previous history of tuberculosis and chronic hepatitis B had higher risk of SARS-CoV-2 infection.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE AND/OR POLICY

⇒ Efforts must be made to simultaneously vaccinate all individuals residing in congregate residential facilities regardless of age, rather than a phased age-wise implementation.

⇒ Durability beyond 90 days must be investigated in future research that will inform the time for further booster doses.

INTRODUCTION

Vaccines remain the primary tool to contain the COVID-19 pandemic. However, the recent surge of infection globally, the emergence of variants and the varying estimates of vaccine effectiveness based on vaccine type, geography and populations have cast doubts and confusion in the public.[1–7] Uptake is further challenged by resistance and hesitancy from sectors of society having unfavourable perceptions towards vaccines.[8–11] As such, evidence of vaccine effectiveness in the real world in diverse settings and populations including local communities is needed.

India was gripped by a deadly second wave of the COVID-19 pandemic in 2021 as the vaccines were being rolled out. The government prioritised elderly and people with comorbidities to receive COVID-19 vaccines, and then it was made available for other adults.[12 13] This phased roll-out created a setting for natural experiment providing an opportunity to compare outcomes in people who were unvaccinated, who had received the first dose of vaccine and who had received two doses of vaccine. In this study, we determined the prevalence of COVID-19 and effectiveness of Covishield vaccine in congregate living facilities in the Tibetan community in Himachal Pradesh, India, that experienced outbreaks of COVID-19.

METHODS

Population and settings

Delek Hospital is a community hospital and a designated COVID-19 testing and vaccine centre located in Dharamshala, Himachal Pradesh. The hospital attends to Tibetan and local Indian populations in the region and provides service to several residential facilities including monasteries, nunneries, boarding schools and old age homes. Residents interact in close-knit spaces in these institutes and transmission can happen rapidly. During the second wave in India, COVID-19 outbreaks happened in several living facilities in Dharamshala. Residents of all ages in three monasteries, two old age homes, one vocational centre and one language and culture learning centre where outbreaks happened were included in the study.

Study design

Ever since the start of the pandemic, Delek Hospital has been providing testing and prevention services to the boarding schools, monasteries, nunneries and other residential facilities in Dharamshala. Starting December 2020, the institutes have been actively monitored for outbreaks of COVID-19 using a surveillance system. COVID-19 task force at the Delek Hospital carried out regular follow-up of the residents of the congregate settings supported by healthcare workers of the respective institutes. A COVID-19 surveillance database was used to capture relevant data including vaccine administration and test results. Only Covishield (Oxford/AstraZeneca) vaccine was used. During outbreak in an institute, all residents were considered contacts and tested for COVID-19. Residents would receive COVID-19 tests either at Delek Hospital or at the residential facility itself carried out by the task force. Testing for SARS-CoV-2 was done using real-time reverse transcriptase PCR (RT-PCR) assays or rapid antigen test (RAT) on nasopharyngeal swabs. RT-PCR testing was carried out at a nearby Government Medical College Hospital. All persons detected with SARS-CoV-2 infection were quarantined at the institute itself or at a designated quarantine centre. Persons with severe COVID-19 or those identified as needing further care were referred to a tertiary care centre. The COVID-19 taskforce staff conducted interviews to obtain the sociodemographic and clinical information.

Exposure

Receipt of vaccine against COVID-19 was the exposure variable. A resident was either unvaccinated, had received one dose or had received two doses of Covishield vaccine. A unique participant identifier was used to link subsequent vaccine administration and testing data to a participant.

Outcome

Primary outcome was vaccine effectiveness, evaluated through the development of COVID-19 across the categories of exposure. A COVID-19 outcome was restricted to those episodes occurring after first or second dose of Covishield vaccine. Episodes of COVID-19 prior to the first dose of vaccine administration was classified as a 'previously exposed or past COVID-19' case. The study's secondary outcome, also referred to as 'unfavourable outcome' henceforth, was composite, consisting of shortness of breath (or use of supplemental oxygen), hospitalisation or death due to COVID-19.

Covariates

Demographic and clinical history that were recorded included age, sex, occupation, place of residence, current smoking status, history of tuberculosis (TB), presence of chronic obstructive pulmonary disease (COPD), cardiovascular disease (CVD) (heart disease, stroke or hypertension), diabetes mellitus, chronic hepatitis B virus (HBV) and chronic kidney disease (CKD). For those testing positive for SARS-CoV-2 infection, information on symptoms—cough, fever, shortness of breath, loose stool, loss of smell, loss of taste—were collected. Given the relatively short study period, covariates were not time-updated and the same values as that at the baseline were assumed over the course of the study. For example, age at baseline or presence or absence of a comorbidity at

baseline was assumed to remain so for the duration of the study.

Statistical analysis

Participants are identified in the electronic surveillance database by a unique identifier. Date of enrolment into the database at the time of outbreak, date of receipt of Covishield vaccine dose(s) and date of COVID-19 outcome were temporally ordered to enable causal inference. The primary exposure variable was categorised into those (1) unvaccinated, (2) received first dose of Covishield and (3) received two doses of Covishield. The exposure variable was time-updated, coded as '0' for unvaccinated; as '1' for those who have received one dose only; and for individuals who have received two doses of the vaccine, the exposure variable was coded as '1' for the time from the date of receipt of the first dose up until the date of receipt of the second dose and '2' for the time from the date of receipt of the second dose up until the end of the follow-up period. The outcome was accordingly attributed. To assess effectiveness of the first dose of Covishield, the outcome of interest constituted prospective COVID-19 cases developing after receipt of the first dose of vaccine but before receipt of the second dose. To assess the effectiveness of the second dose, the outcome constituted prospective cases developing after the second dose of Covishield. Additionally, to assess interval-specific effectiveness of Covishield after first dose, an ordinal exposure variable was generated consisting of the following categories: (1) unvaccinated (reference), (2) interval of 14–29 days from the first dose of vaccine, and (3) interval of 30–59 days. Because of inadequate exposure time, effectiveness associated with the the first dose beyond 60 days and with the categorical time intervals after the second dose of Covishield vaccine was not possible. Individuals who have had a positive test for COVID-19 before receipt of the first dose of Covishield vaccine were considered previously exposed. The secondary outcome, which was a composite outcome comprised of use of supplemental oxygen or shortness of breath, hospitalisation or death, was also assessed based on receipt of Covishield. Time scale for the participants was defined in terms of observed time-on-study in calendar months, with 20 February 2021 being the earliest start date of vaccine administration for the institutes. Participants started contributing exposure time after the receipt of the first dose of the vaccine. Vaccines were implemented for the institutes at different times, and hence, the start of follow-up period was different for the participants based on the time of vaccine implementation for the residential facility. Episodes of COVID-19 prior to receipt of vaccine were considered as 'previous COVID-19' and not included as an outcome. Participants were censored at the earlier of the first development of the outcome, or administratively on 31 July 2021. HRs were generated using Cox proportional hazard regression comparing the time to development of the outcome between the exposure categories. Effectiveness of the vaccine (%) is then calculated as (1−HR)×100. Because of the dependence of outcomes within the residential facilities, we used the Huber-White robust SE to account for clustering. Given that age and residence type may be correlated with the exposure variable, we checked for collinearity of the cofactors by calculating the variance inflation factor (vif) and tolerance (1/vif) post regression. Data were processed and analysed using STATA (Stata/BE V.17.0) software (StataCorp, College Station, Texas, USA).

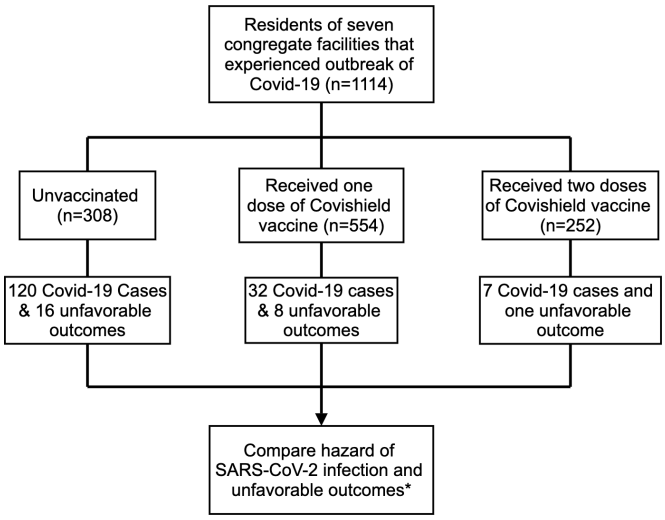

Figure 1 Defining the cohort to determine effectiveness of Covishield vaccine against SARS-CoV-2 infection. *Unfavourable outcome defined as either death, hospitalisation or use of supplemental oxygen.

Patient and public involvement

Patients or members of the public are not involved in the design, or conduct, or reporting or dissemination plans of the research.

Ethics approval

This study has been exempted by the Delek Hospital's Ethics Committee and the Johns Hopkins Medicine Institutional Review Board as an urgent public health initiative with the need for informed consent from individual participants waived.

RESULTS

COVID-19 outbreaks

Between December 2020 and July 2021, seven residential facilities in Dharamshala have experienced at least one outbreak (figure 1); two institutes have experienced two outbreaks. The point prevalence of COVID-19 during the outbreaks ranged from 11% to 57% in the individual facilities (figure 2A). The prevalence decreased with increasing age categories, which was in accordance with higher vaccination rates in older age residents (figure 2B). Most outbreaks (n=5) occurred in the month of May when India was facing the second wave of the pandemic. There occurred a total of 341 COVID-19 cases during the outbreaks. A total of 1145 COVID-19

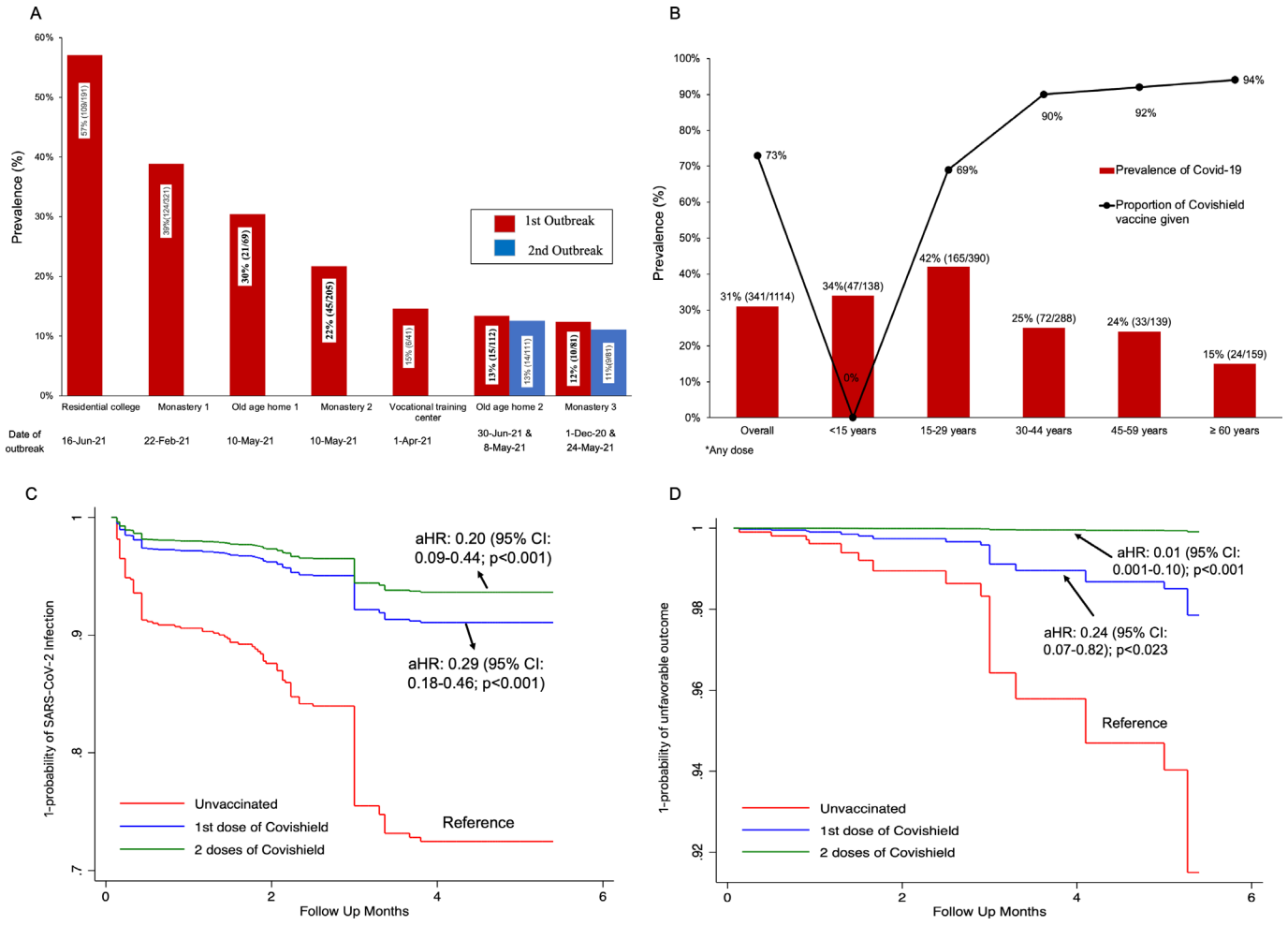

Figure 2 (A) Prevalence of COVID-19 in congregate residential facilities during outbreaks in Northern India (December 2020–July 2021). (B) *Covishield receipt and age-wise prevalence of COVID-19 during outbreaks in congregate facilities in Northern India (December 2020–July 2021). (C) Effectiveness of Covishield against SARS-CoV-2 infection. (D) Effectiveness of Covishield against unfavourable COVID-19 outcomes. aHR, adjusted HR.

tests were carried out; 966 were RT-PCR-based tests and 179 were RAT.

Baseline characteristics

Between 1 December 2020 and 31 January 2021, 1114 residents from seven residential facilities—two old age homes (n=183), three monasteries (n=636) and two learning centres (n=295)—were enrolled into the study (table 1). Of the 1114 residents, 27.6% (n=308) were unvaccinated, 49.7% (n=554) had received only one dose of Covishield and 22.6% (n=252) had received two doses of Covishield vaccine (figure 1). Median age (IQR) of the residents was 31 (19–46) years; 12.4% (n=138) were children <15 years, 73% (n=817) were between 15 and 59 years and 14% were aged ≥60 years. None of the children were vaccinated, whereas 80% of residents between 15 and 60 years and 94% of residents above 60 years had received either one or two doses of Covishield vaccine. Majority (82%, n=914/1114) of the residents were males; this was because three of the seven facilities were monasteries. Greater proportion of females were vaccinated as compared with males (80.5% vs 70.6%; p=0.004). Of the comorbidities among residents, hypertension (10%) was most prevalent followed by chronic hepatitis B (5.9%), diabetes mellitus (3.2%), current smoking (2.9%), COPD (1.6%) and CVD (1.5%). History of TB was prevalent (11%). Compared with residents without comorbidities, those with comorbidities were more likely to be vaccinated (table 1).

COVID-19 outcomes

Of the 341 COVID-19 cases that occurred in the residential facilities during the outbreaks, 159 cases developed prospectively after start of vaccination. Incidence proportion of COVID-19 was 4.8% (n=39/807) in the vaccinated residents and 40% (n=120/308) in the unvaccinated residents. In bivariate analyses, residents who received Covishield vaccine had higher frequency of cough (46% vs 22%; p=0.003) and fever (41% vs 20%; p=0.009) as compared with those who did not. Frequency of shortness of breath was lower in vaccinated than unvaccinated residents (9% vs 18%; p=0.113). Of those who developed COVID-19, 51% (n=75) were asymptomatic. There was no significant difference in the cumulative incidence of

Table 1 Baseline and clinical characteristics of residents of congregate facilities that experienced outbreaks of COVID-19 between 1 January and 31 July 2021 in India

Characteristics	All residents (n=1114), %	Unvaccinated (n=308)	1st or 2nd doses of Covishield vaccine (n=806)	P value (χ^2 or ANOVA)
Age, median (IQR)	31 (19–46)	15 (11–18)	38 (26–51)	<0.001
Age				
<15 years (n=138) 15–59 years (n=817) ≥60 years (n=159)	12.4% 73.3% 14.3%	138/138 (100%) 161/817 (19.7%) 9/159 (5.7%)	0 (0.0%) 656/817 (80.3%) 150/159 (94.3%)	<0.001
Male (n=914) Female (n=200)	82% 18%	269/914 (29.4%) 39/200 (19.5%)	645/914 (70.6%) 161/200 (80.5%)	0.004
Residence type				
Old age homes (n=183) Monasteries (n=636) Learning centres (n=295)	16.4% 57.1% 26.5%	39/183 (21.3%) 215/636 (33.8%) 54/295 (18.3%)	144/183 (78.7%) 421/636 (66.2%) 241/295 (81.7%)	<0.001
Current smoker (n=32) Non-smoker (n=1082)	2.9% 97.1%	2/32 (6.3%) 306/1082 (28.3%)	30/32 (93.8%) 776/1082 (71.7%)	0.006
Past TB (n=123) No past TB (n=991)	11% 89%	14/123 (11.4%) 294/991 (29.7%)	109/123 (88.6%) 697/991 (70.3%)	<0.001
Chronic hepatitis B (n=66) No hepatitis B (n=1048)	5.9% 94.1%	6/66 (9.1%) 302/1048 (28.8%)	60/66 (90.9%) 746/1048 (71.2%)	0.001
COPD (n=18) No COPD (n=1096)	1.6% 98.4%	2/18 (11.1%) 306/1096 (27.9%)	16/18 (88.9%) 790/1096 (72.9%)	0.114
CVD (n=17) No CVD (n=1097)	1.5% 98.5%	2/17 (11.8%) 306/1097 (27.9%)	15/17 (88.2%) 791/1097 (72.1%)	0.140
Hypertension (n=111) No hypertension (n=1003)	10% 90%	4/111 (3.6%) 304/1003 (30.3%)	107/111 (96.4%) 699/1003 (69.7%)	<0.001
Diabetes mellitus (n=36) No diabetes mellitus (n=1078)	3.2% 96.8%	2/36 (5.6%) 306/1078 (28.9%)	34/36 (4.2%) 772/1078 (71.6%)	0.003
CKD (n=3) No CKD (n=1110)	0.3% 99.7%	0/3 (0.0%) 308/1110 (100%)	3/3 (100%) 802/1110 (72.3%)	0.565
Previous COVID-19 (n=120) No previous COVID-19 (n=994)	11% 89%	3/120 (2.5%) 305/994 (31.7%)	117/120 (97.5%) 689/994 (69.3%)	<0.001
Symptoms of persons developing COVID-19 (n=159)	**Residents (n=159)**	**Unvaccinated (n=120)**	**1st or 2nd doses of Covishield (n=39)**	**P value (χ2 or ANOVA)**
Cough (n=44) Fever (n=40) Shortness of breath (n=18) Loose stool (n=14) Loss of taste (n=25) Loss of smell (n=29) Any symptom (n=75)	27.7% 25.1% 18.0% 8.1% 15.7% 18.2% 48.7%	26/120 (21.7%) 24/120 (20.0%) 11/120 (9.2%) 9/120 (7.5%) 20/120 (16.7%) 24/120 (20.0%) 51/120 (44.4%)	18/39 (46.2%) 16/39 (41.0%) 7/39 (17.9%) 5/39 (12.8%) 5/39 (12.8%) 5/39 (12.8%) 24/39 (61.4%)	0.003 0.009 0.113 0.308 0.566 0.313 0.063
Hospitalised (n=11) Not hospitalised (n=1103)	1% 99%	4/308 (1.3%) 304/308 (98.7%)	7/806 (0.87%) 799/806 (99.1%)	0.516
Died (n=4) Alive (n=1110)	0.4% 99.6%	3/308 (1%) 305/308 (99%)	1/806 (.12%) 805/806 (99.88%)	0.034

ANOVA, analysis of variance; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; TB, tuberculosis.

hospitalisation by vaccine status. There were four deaths; three happened in the unvaccinated group, all in residents aged >60 years. The cumulative incidence of death was higher in the unvaccinated residents (1% vs 0.12%; p=0.034).

Association of covariates and COVID-19 outcomes

Median age of the residents who developed COVID-19 was 18 (IQR 13–31) years. Younger age was associated with higher risk of SARS-CoV-2 infection (adjusted HR (aHR) 1.02; 95% CI 1.01 to 1.03; p=0.002). Older age was associated with higher risk of unfavourable outcomes (aHR 1.04; 95% CI 1.01 to 1.06; p=0.006) (table 2). Vaccine coverage was 94% for persons >60 years of age, 42% for persons between 14 and 29 years and 0% for children less than 15 years of age. On modelling the risk of infection based on the type of residence that is, monastic settings, residential colleges and old age homes, we observed greater risk for the residential colleges as

Table 2 Multivariate analyses to determine relationship between baseline or clinical characteristics and risk of COVID-19 and adverse outcomes in residents of congregate living facilities in India between 1 January and 31 July 2021

Characteristics of residents	Residents detected with SARS-CoV-2 infection (n/N, %)	Risk of SARS-CoV-2 infection		Risk of unfavourable COVID-19 outcomes*	
		†aHR (95% CI)	P value	†HR (95% CI)	P value
Median age (IQR)	18 (13–31)	0.98 (0.97 to 0.99)	0.002	1.04 (1.01 to 1.06)	0.006
Male Female	125/914 (13.7%) 34/200 (17.0)	0.75 (0.50 to 1.11) Reference	0.148	2.62 (0.73 to 9.50) Reference	0.141
Type of living facility					
Old age homes Monasteries Other facilities‡	21/183 (11.5%) 79/636 (12.4%) 59/295 (20.0%)	Reference 0.81 (0.48 to 1.33) 1.71 (1.11 to 2.65)	0.421 0.016	Reference 2.51 (0.73 to 8.53) 9.33 (3.31 to 26.30)	0.691 <0.001
Past tuberculosis No past tuberculosis	16/123 (13.0%) 143/991 (14.4%)	1.62 (1.004 to 2.61) Reference	0.047	1.30 (0.49 to 3.44) Reference	<0.599
CVD No CVD	6/115 (5.3%) 153/999 (15.3%)	1.27 (0.49 to 3.26) Reference	0.624	2.17 (0.56 to 8.39) Reference	0.261
Diabetes mellitus No diabetes mellitus	1/36 (2.8%) 158/1078 (14.7%)	0.38 (0.05 to 2.81) Reference	0.350	1.10 (0.28 to 4.36) Reference	0.889
COPD No COPD	6/18 (33.3%) 153/1096 (14.0%)	3.12 (1.47 to 6.63) Reference	0.003	9.25 (3.50 to 24.47) Reference	<0.001
Chronic hepatitis B No chronic hepatitis B	10/66 (15.2%) 149/1048 (14.2%)	1.78 (1.04 to 3.02) Reference	0.034	1.63 (0.60 to 4.43) Reference	0.333
Current smoker Not current smoker	5/32 (15.6%) 154/1082 (14.2%)	1.59 (0.63 to 4.02 Reference	0.331	–	–
Previous COVID-19 No previous COVID-19	0/120 (0.0%) 159/994 (16%)	–	–	–	–

*Unfavourable outcomes defined as shortness of breath or use of supplemental oxygen, hospitalisation or death.
†Adjusted for age, sex, residence type, current smoking status, hypertension, diabetes, chronic obstructive pulmonary disease, cardiovascular disease and chronic hepatitis B virus infection.
‡Other facilities include one vocational centre and one residential college where language and culture are taught.
COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease.

compared with the old age homes (aHR 1.71; 95% CI 1.11 to 2.65; p=0.015). This is in accordance with the greater proportions of unvaccinated youth residents in the colleges. No relation was observed between gender and risk of SARS-CoV-2 infection or worse clinical outcomes. Previous history of TB was associated with a higher risk of SARS-CoV-2 infection (aHR 1.62; 95% CI 1.01 to 2.61; p=0.047). Of the comorbidities, COPD was associated with both higher risk of infection (aHR 3.12; 95% CI 1.47 to 6.63; p=0.003) and unfavourable outcomes (aHR 9.25; 95% CI 3.50 to 24.47; p<0.001) and chronic hepatitis B virus (HBV) infection was associated with a higher risk of infection with SARS-CoV-2 (aHR 1.78; 95% CI 1.04 to 3.02; p=0.034). The models for the association of covariates with SARS-CoV-2 infection were adjusted for age, gender, residence type, COPD, CVD, diabetes mellitus, chronic hepatitis B and current smoking history. Eleven per cent (n=120/1114) of the residents had developed COVID-19 prior to receiving first dose of Covishield, none developed recurrent COVID-19.

Vaccine effectiveness

There were 3628 total person-months of follow-up time available for analysis: 1587 person-months for the unvaccinated, 1277 person-months for recipients of one dose, and 764 person-months for recipients of two doses of Covishield. The median number of days elapsed for a participant from the receipt of the first dose until the receipt of the second was 39 days (IQR 35–50 days; range 2–123 days) and from the receipt of the second dose till the end of the follow-up period was 89 days (IQR 15–101; range 10–134 days). Incidence rates of COVID-19 were 76 (95% CI 63 to 90) per 1000 person-months for the unvaccinated, 25 (95% CI 18 to 35) per 1000 person-months for those who received one dose and 9 (95% CI 4 to 19) per 1000 person-months for those who received two doses. On multivariate analysis, we found lower hazard of COVID-19 for persons who received one dose of Covishield (aHR 0.29; 95% CI 0.18 to 0.46; p<0.001) and for persons who received two doses of Covishield (aHR 0.20; 95% CI 0.09 to 0.44; p<0.001), as compared with unvaccinated persons. Based on the HRs, we calculated vaccine effectiveness of 71% (95% CI 54% to 82%) for first dose of Covishield and 80% (95% CI 56% to 91%) for two doses of Covishield. As vaccination efforts were going on simultaneously as the outbreaks were happening, it was possible that participants might have been exposed

to SARS-CoV-2 at the time of vaccination. Therefore, we carried out an additional analysis by restricting outcomes for all participants to 14 days after the date of first and second doses of vaccine. We found greater effectiveness of 93% and 98% after 14 days of first and second doses of Covishield vaccine, respectively (aHR (95% CI) for the first dose: 0.07 (0.03 to 0.15); p<0.001 and aHR (95% CI) for the second dose: 0.02 (0.002 to 0.15); p<0.001). On evaluation of protection against unfavourable outcomes after 14 days of vaccination, we found that one dose of Covishield was 86% effective (aHR 0.24; 95% CI 0.07 to 0.82; p=0.023) and two doses of Covishield was 99% effective (aHR 0.01; 95% CI 0.002 to 0.10; p<0.001).

In a separate model, we assessed the relationship between time elapsed after the first dose of Covishield and SARS-CoV-2 infection. The variable for passage of time after the first dose was categorised as 14–29 days and 30–60 days. We observed no protection against infection for the interval of 14–30 days. However, the protection was marked between 30 and 60 days (aHR 0.01; 95% CI 0.002 to 0.10; p<0.001), showing vaccine effectiveness of 99% (95% CI 90% to 99.9%). There was insufficient power to assess effectiveness beyond 60 days. On conducting a sensitivity analysis by excluding residents with previous history of COVID-19, we did not observe meaningful difference in vaccine effectiveness against SARS-CoV-2 infection for first (HR 0.32; 95% CI 0.20 to 0.51; p<0.001) and second doses (HR 0.22; 95% CI 0.10 to 0.48 p<0.001) of Covishield. All the above models were adjusted for age, gender, residence type, history of TB, COPD, CVD (including hypertension), diabetes mellitus, chronic hepatitis B and current smoking history (table 3). We did not encounter concerns of collinearity between variables included in regression model (mean vif: 1.26; range of tolerance of individual variables: 0.45 to 0.99).

DISCUSSION

Principal findings

In this study, we have demonstrated the real-world effectiveness of Covishield vaccine against SARS-CoV-2 infection and unfavourable outcomes using data from outbreaks in highly transmissible settings. We observed high point prevalence of COVID-19 ranging from 11% to 57% in the congregate living facilities during the second wave of the pandemic in India. The incidence rate of COVID-19 was ninefold higher in the unvaccinated as compared with the recipients of two doses of the vaccine (76/1000 person-months vs 9/1000 person-months) and of those who developed COVID-19, 51% had asymptomatic infection. Transmission was common in the younger age group which was evident from the lower median age of the infected persons, that is, 18 years, than the overall median age of all participants, which was 31 years. The first and second doses of Covishield were 71% and 86% effective, respectively, in protecting against SARS-CoV-2 infection in the first 3 months after vaccine administration. The effectiveness of the first and second doses of Covishield were higher, 93% and 98% respectively, after 14 days of administration. We found that two doses of Covishield reduces the risk of unfavourable clinical outcomes from COVID-19 including use of supplemental oxygen, hospitalisation or death by 98%.

Results and implications

Our findings largely conformed with that of other observational studies and clinical trials. In a large VIN-WIN cohort of ~1.5 million healthcare workers in India, vaccine effectiveness——after 2 weeks of vaccine administration—of 94% and 92% were observed for recipients of one and two doses of Covishield.[14] Although the results of the VIN-WIN cohort were not adjusted for potential confounders, the large sample of the study was valuable. In another large real-world study in England, vaccine effectiveness after 28–35 days of administration of first dose of ChAdOx1-S (Oxford-AstraZeneca, equivalent of Covishield) was 60%–73% for persons above 70 years of age.[15] Furthermore, a large prospective cohort study of ~1.3 million people in Scotland has shown that the first dose of ChAdOx1-S vaccine was 88% effective in protecting against hospitalisation between 28 and 35 days after administration.[16] In a pooled analysis of data from four randomised controlled trials in UK, Brazil and South Africa, effectiveness of ChAdOx1-S between 55% and 81% was observed depending on the duration of prime-boost interval with longer interval associated with greater effectiveness.[17] The higher effectiveness observed in this study may be attributable to the younger age of the participants in this study—86% were below 60 years with median age of 31 years. Additionally, a high baseline prevalence of past COVID-19 history in the vaccinated residents may have boosted the immunity.

We did not observe a protective effect against SARS-CoV-2 infection in the first 30 days of vaccination. This may be due to the following reasons: First, residents at the time of vaccination might already have been exposed to SARS-CoV-2. Vaccination drives were ongoing in India at the time of the study. Second, elderly persons and persons with comorbidities were selected to receive the vaccine first; prevalence of comorbidity and symptomatic COVID-19 were higher in them (table 1).[18] This could imply a greater baseline susceptibility for the vaccinated group to spuriously drive down vaccine effectiveness toward null. Third, greater immunogenicity of Covishield vaccine has been documented after few weeks of vaccine administration.[17 19]

Our finding of greater risk of infection and unfavourable outcomes associated with COPD is consistent with the existing literature. A lack of statistically significant association between cardiovascular disease and SARS-CoV-2 infection or unfavourable outcomes may be due to inadequate sample size as majority of participants in the study were of young age. We observed a statistically significant higher risk of SARS-CoV-2 infection in persons with previous history of TB. We are not aware of a prior study documenting this association but instead, studies

Table 3 Effectiveness of Covishield vaccine against SARS-CoV-2 infection and COVID-9 outcomes in residents of congregate living facilities in India

Exposure group	Person-months of follow-up	*COVID-19 cases (n)	Incidence rate (95% CI) per 1000 person-months	†aHR for COVID-19 (95% CI); P value	‡VE (%)	§Unfavourable outcomes (n)	aHR for unfavourable outcomes (95% CI); P value
Unvaccinated (UV)	1587	120	76 (63 to 90)	Reference	–	16	Reference
First dose of Covishield vaccine	1277	32	25 (18 to 35)	0.29 (0.18 to 0.46; p<0.001)	71% (54%–82%)	8	0.24 (0.07 to 0.82; p=0.023)
Two doses of Covishield vaccine	764	7	92 (44 to 19)	0.20 (0.09 to 0.44; p<0.001)	80% (56%–91%)	1	0.01 (0.001 to 0.10; p<0.001)
Time interval after 1st Dose							
Unvaccinated	1587	120	76 (63 to 90)	Reference	–	–	–
14–29 days	54	6	111 (50 to 247)	0.92 (0.38 to 2.26; p=0.858)	–	–	–
30–60 days	925	1	1 (0.2 to 7.7)	0.01 (0.002 to 0.10; p<0.001)	–	–	–

*COVID-19 cases for vaccine effectiveness analysis were restricted to those happening after the first or second dose of vaccine. Therefore, total cases (n=159) in this table differ from that of figure 2D (n=341).
†HR adjusted for age, sex, residence type, current smoking status, hypertension, diabetes, chronic obstructive pulmonary disease, cardiovascular disease and chronic hepatitis B virus infection.
‡Vaccine effectiveness = (1–HR)×100%.
§Unfavourable clinical outcomes defined as those developing shortness of breath/use of supplemental oxygen, hospitalised or who died after 14 days of vaccine administration.
aHR, adjusted HR.

in the past have suggested inverse relation between prior TB history or BCG vaccine and risk of COVID-19.[20 21] In the context of the conflicting findings, and a significant morbidity and mortality for coinfected patients,[22] the TB-COVID-19 relationship should be further investigated. Our finding of increased risk of SARS-CoV-2 infection for those with previous TB could be associated with a greater susceptibility secondary to post-TB lung damage. An additional finding of this study has been that persons with chronic HBV infection were observed to have higher risk of SARS-CoV-2 infection. Most studies to date have described adverse clinical outcomes for persons with SARS-CoV-2 and chronic HBV coinfection.[18 23] However, it is unclear how infection with HBV influences the risk of SARS-CoV-2 infection; few studies have suggested a lower risk of infection for persons with chronic HBV infection prompting speculation on the possibility of 'immune exhaustion' as a result of long standing infection with HBV.[23 24] However, these studies were from the early phases of the pandemic in 2020. Given the constant evolution of the variants, further investigations to study the relationship between COVID-19 and chronic HBV are urgently needed.

We did not calculate HR for events that occurred within 14 days of vaccine receipt because for one institute, there was an active outbreak of COVID-19 happening simultaneously as the vaccination was being administered. This meant that many of the residents might already be exposed and likely infected at the time of receiving the vaccine, but unaware of the infection status as the test results took time to come. It was likely that the knowledge and fear of the risk of exposure might have selectively driven the exposed participants to receive the vaccine. Therefore, for reasons based on temporal alignment and causal inference, calculating the hazard for participants for this specific interval could result in biased estimates of the true effect of vaccine. Barring this one institute, none of the institutes had recorded COVID-19 in the first 14 days of vaccine administration. We have arbitrarily decided to use '14 days' as the cut-off because vaccine administration would usually be complete for all the residents by that time.

Strengths and limitations

A key strength of the study is its prospective and population-based nature where all residents of the institutes were assessed for exposure and outcome that could ensure a stronger causal inference. The study population included all age groups giving it generalisability, especially for those aged 15–59 years old that constituted majority of the participants. An additional strength has been the characterisation of COVID-19 outbreak in residents of congregate facilities that could be reflect the situation in many other settings where people live together in close-knit spaces. This is the first study to document the COVID-19 status and vaccine effectiveness in congregate facilities of Tibetan refugees in India, a highly vulnerable population group.

While we could not type the SARS-CoV-2 strains, the outbreaks happened during the second wave of the pandemic in India that was largely driven by the Delta variant (B.1.617.2). Therefore, it may be reasonable to associate the findings from this study to that caused by the Delta variant of SARS-CoV-2. A limitation could be the relatively smaller sample that prevented us from assessing the outcome of hospitalisation or death separately, and limited follow-up time precluding calculation of vaccine effectiveness beyond 60 days.

CONCLUSIONS

We conclude that the first and second doses of Covishield vaccine were highly effective in preventing SARS-CoV-2 infection in highly transmissible settings, mitigating disease severity and preventing death. With accrued person-time, we expect to describe the effectiveness stratified by age, prime-boost and post-boost time intervals with greater confidence.

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