Original Article

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Effectiveness of the ChAdOx1 nCoV-19 Vaccine against Laboratory-confirmed Cases of COVID-19: A Test-negative Case-control Study from Central Kerala, India

Community Section

GEETHADEVI MADHAVIKUTTY[1], AJITH RAVEENDRAN[2], RONNIE THOMAS[3], ASHA JOAN MURALI[4], ANJU CHEMPAKASSERIL MATHEW[5], ANUPA LUCAS[6], SOBHA AKSHAYAKUMAR[7]

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ABSTRACT

Introduction: The COVID-19 pandemic continues to impact livelihoods worldwide, and in the absence of specific antivirals, the vaccine remains the main weapon against it. Assessing the effectiveness of vaccines against Coronovirus Disease 2019 (COVID-19) in practice is crucial as COVID-19 variants continue to emerge, and public health decisions must be supported by scientific risk-benefit considerations.

Aim: To determine the Vaccine Effectiveness (VE) of two doses of the ChAdOx1 nCoV-19 (Covishield) vaccine in preventing laboratory-confirmed COVID-19.

Materials and Methods: A test negative case control design was used to determine the VE in total of 702 individuals which included 351 laboratory confirmed cases using Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) and 351 controls who tested negative among those who attended the testing sites of the Urban Family Health Centre of Government Medical College Kottayam, Kerala, India from July 2021 to September 2021. Details regarding vaccination status, sociodemographic factors, symptoms, and co-morbidities were collected from consented and eligible participants. The collected information was entered into a proforma, which was later entered into MS Excel and analysed using R software version 4.1.3. The groups were compared using binary logistic regression to calculate the adjusted Odds Ratio (aOR) with adjustment for gender, age group, education, occupation, presence of symptoms, and co-morbidity status. VE% was calculated as 100 * (1-aOR).

Results: The median age (interquartile range) of cases and control was 44 (33-57) years and 50 (35-60) years, respectively. The VE of two doses of the ChAdOx1 nCoV-19 vaccine in protecting against laboratory-confirmed COVID-19 was 87% (95% CI 78-92), with an aOR of 0.13. A separate analysis was conducted to determine the VE among symptomatic individuals, which showed a VE of 89% (95% CI 79-94), with an aOR of 0.11.

Conclusion: Two doses of the ChAdOx1 nCoV-19 vaccine are protective against laboratory-confirmed cases of COVID-19.

Keywords: Antivirals, Coronavirus disease 2019, Covishield vaccine, Reverse transcriptase polymerase chain reaction

INTRODUCTION

The COVID-19 pandemic has overwhelmed healthcare systems worldwide [1]. The social and economic disruption associated with it was unprecedented, ultimately pushing millions into poverty [2]. India adopted a containment strategy in the early stages of the pandemic by enforcing a phased lockdown. However, with the rapid spread of infections, the government shifted to vaccination as its primary strategy to mitigate COVID-19. The Delta variant (B.1.617.2), first identified in Maharashtra, India in December 2020, caused the epidemic to rebound [3]. The relaxation of restrictions, followed by the assembly elections held across five states, including Kerala, India in May 2021, accelerated the rate of infection. By the month of June 2021, Delta became the predominant variant, overtaking the Alpha variant (B.1.1.7) [4]. Since then, India has been recording around three lakh cases of COVID-19 per day [5].

The first vaccine to receive emergency use approval in India was the ChAdOx1 nCoV-19 vaccine from Astra Zeneca [6]. At first, vaccination was prioritised for healthcare workers, frontline workers, and the elderly, and by May 2021, the government issued a directive to expand eligibility for all individuals aged 18 years or older. The phase 2/3 clinical trial demonstrated an overall vaccine efficacy of 70.4% after two doses and protection of 64.1% after at least one standard dose against symptomatic disease [7]. Literature has emerged that offers contradictory findings. Recent evidence suggests that the protection against symptomatic disease is mixed, with some studies reporting reduced effectiveness, whereas others suggest very high levels of over 88% [8,9]. What has been known about the effectiveness is largely based on observational studies that report lower effectiveness against infection for the Delta variant compared with the original strain among both partly and fully vaccinated individuals [10,11]. However, these results were based on hospitalisation data, and it is unclear if factors like healthcare-seeking behaviours, population heterogeneity, socio-economic status, etc., played a role.

In general, establishing the real-world effectiveness of mass vaccination programs helps in informed benefit-risk considerations [12]. As Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) variants are emerging, debate continues about the best strategies for the management of the pandemic. The immune escape potential of the Variants of Concern (VoC) and the need for booster doses have become central issues. A key policy priority should, therefore, be to measure VE in real-world settings so that policy makers can decide which vaccination strategies are most appropriate to implement in their context. In Kerala, timely pandemic preparedness and the trace-test policy in the early stages of the pandemic limited outbreak size [13]. This, along with high primary vaccination coverage, makes the southern state's containment strategy a different story. To inform policy on vaccination and focused containment measures in Kerala,

the present study attempts to examine the field level of real-world effectiveness of the ChAdOx1 nCoV-19 vaccine against laboratory-confirmed infection.

MATERIALS AND METHODS

A test negative case control design was used to determine VE in total of 702 individuals which included 351 laboratory confirmed cases using Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) and 351 controls who tested negative among those who attended the testing sites of the Urban Family Health Centre of Government Medical College, Kottayam, Kerala, India from July 2021 to September 2021. The study was approved by our Institutional Review Board (IRB No: 66/2021 dated 30-4-2021), and all participants provided oral informed consent.

Sample size calculation: The sample size was calculated using the formula for a case-control test-negative design as per the World Health Organisation (WHO) document [15]. $N1=(z/d)^2$ {1/A(1-A)+1/CP2 (1-P2)} Where C is the control-to-case ratio; P2 denotes the prevalence of vaccine exposure in the control group (i.e., vaccine coverage in the population being studied); A=P2 (1-VE)/{1-P2 (VE)} where VE denotes the anticipated VE; z denotes the (1-α) percentage point of the standardised normal distribution (normally this is based on an α=0.05 and thus z=1.96); and d is determined by solving the equation W(β,d)=exp(β)exp(d)-(exp(-d)) where d=zσ and W(β,d) denotes the CI width, i.e., the difference between the upper and lower limits. The number of controls needed is then calculated as C*N1 [15]. Considering a vaccine coverage of 50%, VE of 70%, precision of 10%, and type I error of 5%, and a case-control ratio of one, the minimum number of cases and controls in a case-control design was calculated as 346 each [15]. As the study was based on a test-negative case-control design, cases and controls were selected from these testing sites.

Inclusion criteria: Individuals aged 18 years and above, reporting with Influenza-like Illness (ILI) or Severe Acute Respiratory Infection (SARI) in the area, or primary contacts of cases on quarantine who have done RT-PCR tests in the Urban Family Health Centre testing sites.

Exclusion criteria: Individuals residing outside the study setting, individuals with unknown vaccination status, and individuals who received vaccines other than the ChAdOx1 nCoV-19 vaccine were excluded.

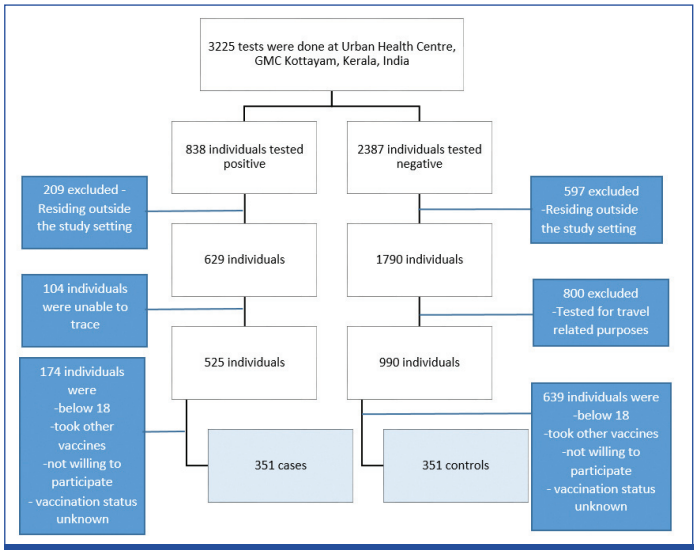
Study Procedure

The Urban Family Health Centre caters to a population of 51,029 spread over 35 wards. As part of surveillance against COVID-19 disease, this Centre has been conducting regular RT-PCR and Antigen testing. A Rapid Response Team (RRT) was functional in each ward, which comprises health workers, voluntary workers, ward councilors, and members from social organisations. Anyone suffering from fever, cough, breathlessness, or any symptom that falls under the case definitions of COVID-19 was traced and brought to a testing facility. Tracing and testing were also done for those who were primary contacts of cases. Vaccination started in institution on January 16, 2021, based on guidelines issued by the Government of India [14], in a phased manner prioritising healthcare workers and frontline workers initially, which extended to those aged 60 years and above and those aged 45-60 years with co-morbidities (since, March 1, 2021), then to all aged 45 years and above (April 1, 2021), and finally to all adults above 18 years (since May 1, 2021).

Cases were defined as participants who tested positive for active SARS-CoV-2 infection by RT-PCR test conducted from July 2021 to September 2021, and controls were defined as those who tested negative for SARS-CoV-2 by RT-PCR test during the same period. The specimen for testing was collected within 10 days of the onset of symptoms or 10 days of quarantine.

Data on vaccination status, presence of symptoms, co-morbidities, and socio-demographic factors were collected through telephonic interviews with each case and control.

A total of 3,225 tests were conducted at the Urban Health Centre from July to September 2021. Out of these, 838 tested positive. To recruit 351 cases and 351 controls, authors contacted 525 cases (response rate 66.8%) and 990 controls (response rate 35.45%), as shown in [Table/Fig-1]. Data on vaccination status was confirmed by verifying the message received in the beneficiary's phone number or the vaccination certificate sent by the participants. Vaccination status was categorised as fully vaccinated, vaccinated with one dose (partially vaccinated), and unvaccinated. Fully vaccinated was defined as individuals who had received a second dose of the ChAdOx1 nCoV-19 vaccine 14 days before RT-PCR testing. Partially vaccinated individuals had received the first dose of the vaccine 14 days before RT-PCR testing. Unvaccinated individuals had not received the vaccine at the time of RT-PCR testing. Individuals who underwent RT-PCR testing within 14 days of the first dose were considered unvaccinated, and those who underwent RT-PCR testing within 14 days of the second dose were considered partially vaccinated. A separate subgroup analysis was conducted for symptomatic individuals to assess the VE in that group. This group comprised 176 cases and 170 controls.



[Table/Fig-1]: Flowchart showing the recruitment of study participants.

STATISTICAL ANALYSIS

The information collected was entered into a proforma and later transferred to MS Excel for analysis using R software version 4.1.3. The Chi-square test was used to compare baseline characteristics between cases and controls. Univariate analysis and multivariate logistic regression were conducted to calculate crude and aORs. Crude and aORs were calculated for the fully vaccinated group versus the unvaccinated group, as well as the partially vaccinated group versus the unvaccinated group. The odds ratio was obtained by taking the exponential function of the regression coefficient from the binary regression model. A multivariate model was developed to account for potential confounding variables, including age, gender, occupation, and socio-economic status. Vaccine Effectiveness percentage (VE%) was calculated as 100*(1-aOR). A subgroup analysis was performed on 346 symptomatic individuals to calculate the crude and aOR for VE% in the fully vaccinated versus unvaccinated group.

RESULTS

A total of 702 individuals, consisting of 351 cases and 351 controls, were included in the study from July to September 2021. A total of 3,225 tests were conducted during this period, with 838 positive results. After exclusions and obtaining consent, 351 patients were

selected for the study [Table/Fig-1]. The median age (interquartile range) of cases and controls was 44 (33-57) and 50 (35-60) respectively. The distribution of gender and co-morbidity was similar between cases and controls (p>0.05) [Table/Fig-2]. Among cases, 323 (92.02%) had mild symptoms and only required outpatient care and home isolation. One death was reported among cases, and Intensive Care Unit (ICU) admission was required for four cases and one control.

Characteristic	Cases n=351	n (%)	Controls n=351	n (%)	p-value
Age categories (in years)					
18-44	178	50.7	137	39	
45-59	97	27.6	120	34.2	
Above 60	76	21.7	94	26.8	
Gender					
Male	173	49.3	166	47.3	0.28*
Female	178	50.7	185	52.7	
Co-morbidity					
Yes	131	37.3	124	35.3	0.871*
No	220	62.7	227	64.7	
COVID-19 symptoms at the time of the RT-PCR test					
Yes	324	92.3	206	58.7	0.001*
No	27	7.7	145	41.3	
Time of COVID-19 RT-PCR test					
July	31	8.8	31	8.8	
August	76	21.7	76	21.6	
September	244	69.5	244	69.5	

[Table/Fig-2]: Baseline characteristics of study participants.
$Chi-square test; *p<0.05 is considered as significant
RT-PCR: Reverse transcriptase polymerase chain reaction

The binary logistic regression model estimated the VE for COVID-19 as 26% and 87% for one and two doses of the vaccine, respectively, after adjusting for age, gender, socio-economic status, education, occupation, and co-morbidity [Table/Fig-3]. In the subgroup analysis of symptomatic individuals, the VE associated with two doses of the vaccine was found to be 89% after adjustment for various factors [Table/Fig-3]. Age-stratified VE was also calculated, and the results are presented in [Table/Fig-4].

Vaccination status	Cases	Controls	Crude OR (95% CI)	Adjusted OR* (95% CI)	Vaccine effectiveness % (95% CI)
For all cases and controls (N=702)					
Unvaccinated	93 (26.5)	36 (10.3)	Ref	Ref	
Partially vaccinated	157 (44.7)	78 (22.2)	0.78 (0.48-1.24)	0.74 (0.46-1.19)	26 (-0.19-54)
Fully vaccinated	101 (28.8)	237 (67.5)	0.16 (0.06-0.26)	0.13 (0.08-0.22)	87 (78-92)
For symptomatic cases and controls (n=346)					
Unvaccinated	84 (47.7)	21 (12.3)	Ref	Ref	
Fully vaccinated	92 (52.3)	149 (87.7)	0.154 (0.09-0.266)	0.11 (0.06-0.21)	89 (79-94)

[Table/Fig-3]: Comparison of Vaccine Effectiveness (VE) among cases and controls.
*Adjusted for age, gender, socio-economic status, education, and co-morbidity

Age group (in years)	Vaccination status	Cases	Controls	Crude OR	Adjusted OR*	Vaccine effectiveness %
18-35	Unvaccinated	31 (70.5)	17 (27.9)	Ref	Ref	90.4
	Fully vaccinated	13 (29.5)	44 (72.1)	0.162	0.096	
35-50	Unvaccinated	43 (67.2)	12 (19)	Ref		90.1
	Fully vaccinated	21 (32.8)	51 (81)	0.115	0.099	
50-65	Unvaccinated	13 (26.5)	6 (5.8)	Ref		84.3
	Fully vaccinated	36 (73.5)	98 (94.2)	0.17	0.157	
Above 65	Unvaccinated	6 (16.2)	1 (2.2)	Ref		90.3
	Fully vaccinated	31 (83.8)	44 (97.8)	0.117	0.097	

[Table/Fig-4]: Age-stratified VE of two doses of ChAdOx1 nCoV-19 vaccine against COVID-19.

Furthermore, two other factors were found to be significant in the multivariate model. Participants with lower educational status (aOR 2.51) and those belonging to below-poverty-line families (aOR 1.56) had a two-fold higher risk of testing positive for COVID-19 [Table/Fig-5].

Factors		Cases n=351	Controls n=351	Adjusted Odds Ratio (aOR)	Confidence interval
Age (years)	<65	305 (86.9%)	293 (83.5%)	1.33	0.32-1.71
	>65	46 (13.1%)	58 (16.5%)	Ref	
Gender	Male	173 (49.3%)	166 (47.3%)	1.01	0.683-1.506
	Female	178 (50.7%)	185 (52.7%)	Ref	
Educational status	Below high school	185 (52.7%)	101 (28.8)	2.51	1.16-33.3*
	High school and above	166 (47.3)	250 (71.2)	Ref	
Socio-economic status	BPL	197 (56.2%)	165 (47%)	1.56	1.01-2.27*
	APL	154 (43.8%)	186 (53%)	Ref	
Co-morbidity	Yes	131 (37.3%)	124 (35.3%)	1.53	0.96-2.56
	No	220 (62.7%)	227 (64.7%)	Ref	

[Table/Fig-5]: Other socio-demographic factors associated with COVID-19 infection.
BPL: Below poverty line; APL: Above poverty line; *Significant

DISCUSSION

The present study was the first of its kind to explore real-world VE in Kerala. The VE for two doses of the vaccine was generally consistent with findings from studies conducted elsewhere [Table/Fig-6] [7,16-19]. The VE for two doses of the vaccine in this study was consistent with findings from other studies conducted in India. Singh C et al., reported a VE of 83% (95% CI 75-89) in Patna [19]. Ghosh S et al., and Bhatnagar et al., found VE of 91.8% (95% CI 88.7-94.02) and 85% (95% CI 79-89%), respectively [16,18]. Tsundue T et al., reported a VE of 80% for two doses of the ChAdOx1 nCoV-19 vaccine in Himachal Pradesh [17]. A pooled analysis of four randomised controlled trials by Voysey M et al., also showed a VE of 81.3% (95% CI 60.3-91.2) [7].

Study	Vaccine effectiveness (95% CI)
Singh C et al., [19]	83% (95% CI 75-89)
Ghosh S et al., [16]	91.8% (95% CI 88.7-94.02)
Bhatnagar T et al., [18]	85% (95% CI 79-89%)
Tsundue T et al., [17]	80% (95% CI 0.09 to 0.44)
Voysey M et al., [7]	81.3% (95% CI 60.3-91.2)
Thiruvengadam R et al., [11]	63·1% (95% CI 51·5-72·1)
Pramod S et al., [20]	54% (95% CI 27%-71%)
Murali S et al., [21]	61.3% (95% CI 43.6-73.4)
Victor PJ et al., [22]	65% (95% CI 61%-68%)

[Table/Fig-6]: Comparison of Vaccine Effectiveness (VE) from various studies [7,11,16-22].

In contrast, certain observational studies conducted in India reported lower VE [Table/Fig-6] [11,20-22]. For example, a study of 10,232 individuals among middle-aged individuals reported an overall VE of 61.3% [21], and a study in Vellore, Tamil Nadu, India observed a pooled VE of 54% [20]. A population-based study conducted in

England using a similar design and methodology also reported lower VE compared to the present study [23]. There are several possible explanations for the relatively higher VE observed in present study. The strict adherence to COVID-19 appropriate behaviours by the people of Kerala and the government's decentralised containment strategy may have contributed to the high VE [24]. The correlation between health literacy and vaccine uptake is well established, and adherence to health-related behaviours such as wearing masks and social distancing among the population in Kerala may have resulted in an overestimation of VE [25,26]. Additionally, the relatively better coverage of the COVID-19 vaccination drive across different age groups and social strata in Kerala may have contributed to the higher VE [27]. However, it is important to note that the emergence of the Omicron variant and waning vaccine immunity over time have resulted in a decline in VE, as indicated by recent research [28-31].

The vaccine effectiveness for a single dose in present study was found to be 26%, which is consistent with findings by Murali S et al., from Chennai, Tamil Nadu (VE 28.7%, 95% CI 2.3-50.3) [21]. Although vaccination status is the most important determinant of VE, sociodemographic factors such as being below the poverty line and having a low educational status may provide valuable insights into the population-level effectiveness of the COVID-19 vaccine. Similar findings have been reported by Gaur K et al., [32]. The present study also demonstrated increased VE among symptomatic individuals, which is supported by evidence from diverse populations, geographic regions, and emerging strains [33-36]. Strengths of the current study include the use of a WHO-recommended test-negative case-control design, which takes into account variations in health-seeking behaviour and vaccine accessibility in the community. Additionally, a multivariate statistical model was used to adjust for potential confounders.

Limitation(s)

Firstly, data about the study participants' previous COVID-19 infection status were not collected. Secondly, inherent biases in retrospective studies, such as recall bias, may have been present. Efforts were made to minimise these errors through phone calls by expert doctors and thorough cross-verification of testing results and vaccination status. Finally, it is possible that the voluntary selection of controls has led to an overrepresentation of vaccinated individuals, which may have resulted in an overestimation of vaccine effectiveness.

CONCLUSION(S)

The results of the present study showed that two doses of the ChAdOx1 nCoV-19 vaccine provide protection against laboratory-confirmed cases of COVID-19, with higher protection observed among symptomatic individuals. The finding of high field-level effectiveness after the second dose would enable public health systems to promote two-dose vaccine uptake among vulnerable groups, particularly in the context of emerging variants of concern.

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REFERENCES

[1] Haldane V, De Foo C, Abdalla SM, Jung AS, Tan M, Wu S, et al. Health systems resilience in managing the COVID-19 pandemic: Lessons from 28 countries. Nat Med. 2021;27(6):964-80.
[2] Thomas R, Jacob QM, Raj Eliza S, Mini M, Jose J, Sobha A. Financial burden and catastrophic health expenditure associated with COVID-19 hospitalizations in Kerala, South India. Clinicoecon Outcomes Res. 2022;14:439-46.
[3] PANGO lineages. Lineage B.1.617.2. [Internet]. [cited 2022 Dec 31]. Available from: https://cov-lineages.org/global_report_B.1.617.2.html.
[4] Visaria A, Dharamdasani T. The complex causes of India's 2021 COVID-19 surge. The Lancet. 2021;397(10293):2464.
[5] Weekly epidemiological update on COVID-19-20 July 2021 [Internet]. [cited 2022 Dec 31]. Available from: https://www.who.int/publications/m/item/weekly-epidemiological-update-on-COVID-19-20-July-2021.
[6] Chavda VP, Vihol DR, Solanki HK, Apostolopoulos V. The vaccine World of COVID-19: India's contribution. Vaccines. 2022;10(11):1943.
[7] Voysey M, Costa Clemens SA, Madhi SA, Weckx LY, Folegatti PM, Aley PK, et al. Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: A pooled analysis of four randomized trials. The Lancet. 2021;397(10277):881-91.
[8] Hitchings MDT, Ranzani OT, Dorion M, D'Agostini TL, de Paula RC, de Paula OFP, et al. Effectiveness of ChAdOx1 vaccine in older adults during SARS-CoV-2 Gamma variant circulation in São Paulo. Nat Commun. 2021;12(1):6220.
[9] Bobdey S, Kaushik SK, Sahu R, Naithani N, Vaidya R, Sharma M, et al. Effectiveness of ChAdOx1 nCOV-19 Vaccine: Experience of a tertiary care institute. Med J Armed Forces India. 2021;77(Suppl 2):S271-77.
[10] Seppälä E, Veneti L, Starrfelt J, Danielsen AS, Bragstad K, Hungnes O, et al. Vaccine effectiveness against infection with the Delta (B.1.617.2) variant, Norway, April to August 2021. Eurosurveillance. 2021;26(35):2100793.
[11] Thiruvengadam R, Awasthi A, Medigeshi G, Bhattacharya S, Mani S, Sivasubbu S, et al. Effectiveness of ChAdOx1 nCoV-19 vaccine against SARS-CoV-2 infection during the delta (B.1.617.2) variant surge in India: A test-negative, case-control study and a mechanistic study of post-vaccination immune responses. Lancet Infect Dis. 2022;22(4):473-82.
[12] Patel MM, Jackson ML, Ferdinands J. Postlicensure evaluation of COVID-19 vaccines. JAMA. 2020;324(19):1939-40.
[13] Valsan C, Thomas R, Chirayath JP, Varghese PR, Kuttichira P. COVID-19 Essentials: Preparing health care professionals before the pandemic spread in Kerala, India. Indian J Public Health Res Dev. 2021;12(1):47-52. [cited 2023 Jan 2]. Available from: https://www.semanticscholar.org/paper/COVID-19-Essentials%3A-Preparing-Health-Care-before-Valsan-Thomas/4fe22b7b1316a46653e4e7a5b8cbd8bac537907c.
[14] Government of India. CoWIN Dashboard [Internet]. [cited 2022 Dec 23]. Available from: https://dashboard.cowin.gov.in/.
[15] World Health Organization. Evaluation of COVID-19 vaccine effectiveness: Interim guidance, 17 March 2021. World Health Organization; 2021.
[16] Ghosh S, Shankar S, Chatterjee K, Chatterjee K, Yadav AK, Pandya K, et al. COVISHIELD (AZD1222) Vaccine effectiveness among healthcare and frontline workers of Indian Armed Forces: Interim results of VIN-WIN cohort study. Medical Journal Armed Forces India. 2021;77:S264-70.
[17] Tsundue T, Namdon T, Tsewang T, Topgyal S, Dolma T, Lhadon D, et al. First and second doses of the 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. BMJ Glob Health. 2022;7(5):e008271.
[18] Bhatnagar T, Chaudhuri S, Ponnaiah M, Yadav PD, Sabarinathan R, Sahay RR, et al. Effectiveness of BBV152/Covaxin and AZD1222/Covishield vaccines against severe COVID-19 and B.1.617.2/Delta variant in India, 2021: A multi-centric hospital-based case-control study. Int J Infect Dis. 2022;122:693-702.
[19] Singh C, Naik BN, Pandey S, Biswas B, Pati BK, Verma M, et al. Effectiveness of COVID-19 vaccine in preventing infection and disease severity: A case-control study from an Eastern State of India. Epidemiol Infect. 2021;149:e224.
[20] Pramod S, Govindan D, Ramasubramani P, Kar SS, Aggarwal R, JIPMER vaccine effectiveness study group. Effectiveness of Covishield vaccine in preventing COVID-19 - A test-negative case-control study. Vaccine. 2022;40(24):3294-97.
[21] Murali S, Sakthivel M, Pattabi K, Venkatasamy V, Thangaraj JWV, Shete A, et al. Effectiveness of the ChAdOx1 nCoV-19 Coronavirus Vaccine (Covishield™) in preventing SARS-CoV2 infection, Chennai, Tamil Nadu, India, 2021. Vaccines. 2022;10(6):970.
[22] Victor PJ, Mathews KP, Paul H, Mammen JJ, Murugesan M. Protective effect of COVID-19 vaccine among health care workers during the second wave of the pandemic in India. Mayo Clinic Proceedings. 2021;96(9):2493-94.
[23] Lopez Bernal J, Andrews N, Gower C, Robertson C, Stowe J, Tessier E, et al. Effectiveness of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines on COVID-19 related symptoms, hospital admissions, and mortality in older adults in England: Test negative case-control study. BMJ. 2021;373:n1088.
[24] Pandi-Perumal SR, Gulia KK, Gupta D, Kumar VM. Dealing with a pandemic: The Kerala model of containment strategy for COVID-19. Pathog Glob Health. 2020;114(5):232-33.
[25] Veldwijk J, van der Heide I, Rademakers J, Schuit AJ, de Wit GA, Uiters E, et al. Preferences for vaccination: Does health literacy make a difference? Med Decis Making. 2015;35(8):948-58.
[26] Glasziou P, McCaffery K, Cvejic E, Batcup C, Ayre J, Pickles K, et al. Testing behaviour may bias observational studies of vaccine effectiveness. J Assoc Med Microbiol Infect Dis Can. 2022;7(3):242-46.
[27] Leelavathy M, Messaline S, Ramachandran D, Sukumaran A, Jose R, Noufel AN. Attitude towards COVID-19 vaccination among the public in Kerala: A cross-sectional study. J Family Med Prim Care. 2021;10(11):4147-52.
[28] Piechotta V, Harder T. Waning of COVID-19 vaccine effectiveness: Individual and public health risk. Lancet. 2022;399(10328):887-89.
[29] Horne EMF, Hulme WJ, Keogh RH, Palmer TM, Williamson EJ, Parker EPK, et al. Waning effectiveness of BNT162b2 and ChAdOx1 COVID-19 vaccines over six months since second dose: OpenSAFELY cohort study using linked electronic health records. BMJ. 2022;378:e071249.

[30] Hachmann NP, Miller J, Collier Aris Y, Ventura JD, Yu J, Rowe M, et al. Neutralization escape by SARS-CoV-2 omicron subvariants BA.2.12.1, BA.4, and BA.5. N Engl J Med. 2022;387(1):86-88.
[31] Buchan SA, Chung H, Brown KA, Austin PC, Fell DB, Gubbay JB, et al. Estimated effectiveness of COVID-19 vaccines against omicron or delta symptomatic infection and severe outcomes. JAMA Network Open. 2022;5(9):e2232760.
[32] Gaur K, Khedar RS, Mangal K, Sharma AK, Dhamija RK, Gupta R. Macrolevel association of COVID-19 with non-communicable disease risk factors in India. Diabetes Metab Syndr. 2021;15(1):343-50.
[33] Ranzani OT, Silva AAB, Peres IT, Antunes BBP, Gonzaga-da-Silva TW, Soranz DR, et al. Vaccine effectiveness of ChAdOx1 nCoV-19 against COVID-19 in a socially vulnerable community in Rio de Janeiro, Brazil: A test-negative design study. Clin Microbiol Infect. 2022;28(5):736.e1-e4.
[34] Emary KRW, Golubchik T, Aley PK, Ariani CV, Angus B, Bibi S, et al. Efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 variant of concern 202012/01 (B.1.1.7): An exploratory analysis of a randomised controlled trial. The Lancet. 2021;397(10282):1351-62.
[35] Hyams C, Marlow R, Maseko Z, King J, Ward L, Fox K, et al. Effectiveness of BNT162b2 and ChAdOx1 nCoV-19 COVID-19 vaccination at preventing hospitalisations in people aged at least 80 years: A test-negative, case-control study. Lancet Infect Dis. 2021;21(11):1539-48.
[36] Nordström P, Ballin M, Nordström A. Effectiveness of heterologous ChAdOx1 nCoV-19 and mRNA prime-boost vaccination against symptomatic COVID-19 infection in Sweden: A nationwide cohort study. Lancet Reg Health Eur. 2021;11:100249.

PARTICULARS OF CONTRIBUTORS:
1. Additional Professor, Department of Community Medicine, Government Medical College, Kottayam, Kerala, India.
2. Assistant Professor, Department of Community Medicine, Government Medical College, Kottayam, Kerala, India.
3. Assistant Professor, Department of Community Medicine, Government Medical College, Kottayam, Kerala, India.
4. Assistant Professor, Department of Community Medicine, Government Medical College, Kottayam, Kerala, India.
5. Assistant Professor, Department of Community Medicine, Government Medical College, Kottayam, Kerala, India.
6. Associate Professor, Department of Community Medicine, Government Medical College, Kottayam, Kerala, India.
7. Professor and Head, Department of Community Medicine, Government Medical College, Ernakulam, Kerala, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Geethadevi Madhavikutty,
Panchavadi, Mathilbhagom, Thiruvalla, Pathanamthitta District-689101, Kerala, India.
E-mail: geethadevi22@gmail.com

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