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Article

Effectiveness of the ChAdOx1 nCoV-19 vaccination among COVID-19 patients: a retrospective cohort study

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Abstract: It is currently unknown how effective the COVID-19 vaccine is at preventing new severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections among the general population. The study suggests that a safe and efficient vaccination against the COVID-19 could help manage this pandemic if widely distributed. The present study aimed to investigate the effectiveness of the ChAdOx1 nCoV-19 vaccine in between vaccinated and unvaccinated cohorts. A retrospective multicenter cohort study comprised 1244 COVID-19 positive patients enrolled in this study from three different hospitals among patients who had been appropriately vaccinated or not between April and June 2021. Data were collected by face-to-face survey, and clinical investigations were obtained by observation. Descriptive statistics and the Cox proportional hazard model of survival analysis were performed in the study. Among the participants, 69% of vaccinated cohorts did not require hospitalization, and 97% successfully recovered from the infection. In respect of age, compared with unvaccinated cohorts, the vaccine effectiveness varied from 81% to 92%. The ChAdOx1 nCoV-19 vaccine was more effective among those aged 60-69 years old and reduced 92% hazard of death than the unvaccinated group [HR ratio - 0.081(.036-.179), *P*=0.0001]. The study found the ChAdOx1 nCoV-19 vaccine is highly effective for receivers. The COVID-19 vaccination demonstrated a significant correlation with a reduced probability of disease severity, hospital admission rate, early recovery from illness, and mortality.

Keywords: vaccine effectiveness; ChAdOx1 nCoV-19 vaccine; SARS-CoV-2**;** vaccinated and unvaccinated cohorts; Cox Proportional Hazard Model; severity

1. Introduction

The COVID-19 caused by Severe Acute Respiratory Syndrome Coronavirus -2 has led to a high mortality rate and was declared a public health emergency by The World Health Organization (WHO) (WHO, 2021a). There

have been 15,78550 and 26,8740466 confirmed patients and 28,016 and 53,02962 deaths in Bangladesh as well as globally (till 10 December 2021). Older adults and those with pre-existing health conditions are significantly affected by this following pandemic. In addition, global economic ramifications caused by physical distancing measures are another major consequence, mostly affecting the vulnerable group (WHO, 2021a; Zhou, 2020; Emary *et al.*, 2021). A vaccine is one of the most feasible and cost-effective means to recover from all these catastrophic effects of the pandemic (Poljak and Norrby, 2014). In addition, a vaccine prevents infectious diseases, improves population-level immunity, averts severe disease, and alleviates the current health crisis (Voysey *et al*., 2021). The COVID-19 vaccine can play a vital role in reducing the ongoing pandemic by raising immunity and preventing disease severity. To date, the scientific community has described the clinical course of COVID-19, estimated the burden, and is trying to develop an effective available vaccine (Almuqrin *et al*., 2021).

Consequently, more than 48 vaccines went to clinical evaluation, and the majority of them showed higher efficacy in multiple international randomized trials, such as; 95% for the Pfizer–BioNTech, 70% for the Oxford–AstraZeneca, 94% for the Moderna vaccine (Voysey *et al*., 2021). The benefits of these vaccines have also been tested, followed by the efficacy rate (Sheikh *et al*., 2021; Emary *et al*., 2021; Hsu *et al*., 2021). The evidence for these vaccine's approval was based on a reduction in severe COVID-19 illness. Some recent studies suggest that the COVID-19 disease can be prevented by 70.4%-95% through vaccination (Baden *et al*., 2021; Polack *et al*., 2020), (Voysey *et al*., 2021). In addition, it has been seen that the unvaccinated patients of COVID-19 are at high risk for developing severe conditions, need higher treatment facilities such as oxygen and ICU, and have a longer time to recover (Tleyjeh *et al*., 2021). Another study reported that patients with acute infections with a higher viral content could significantly reduce with the vaccination. Consequently, COVID-19 vaccination, especially with two dosages, reduced new SARS-CoV-2 infections and worked against a high viral load (Pritchard *et al*., 2021). Bangladesh has started to administrate the vaccines (Oxford-AstraZeneca) among general people on a priority basis from February 7, 2021. This vaccine is also known as the Oxford-AstraZeneca adenovirus vaccine and was formerly termed ChAdOx1 nCoV-19 (WHO, 2021b). Considering the shortage supply, the health care workers and older-aged people, particularly those with the underlying medical conditions, were prioritized to receive the vaccines (Voysey *et al.*, 2021). Compared to a 12.1% global vaccination rate, 2.6% of the population has been vaccinated in Bangladesh. Up to July 15, 10.1 million people had been administered the first dose of any COVID-19 vaccine (ChAdOx1 nCoV-19 or Pfizer–BioNTech), and 4.28 million people were fully vaccinated (WHO, 2021a).

To date, there is a dearth of knowledge worldwide regarding the effectiveness of vaccines in comparison with vaccinated and unvaccinated cohorts. However, there are a couple of studies conducted globally that showed the effectiveness of ChAdOx1 nCoV-19 vaccination among the cohort (Bernal *et al.,* 2021; Hyams *et al*., 2021). No study has been conducted in Bangladesh, to explore how vaccines reduce the rate of the need for hospital admission, oxygen therapy as well as the risk of mortality. We hypothesized that patients who have been vaccinated have a lower risk of complications and require less hospitalization and oxygen therapy than those who are not fully vaccinated. Therefore, the present study aims to investigate the effectiveness of the COVID-19 vaccine (ChAdOx1 nCoV-19) among the vaccinated and unvaccinated populations in Bangladesh.

2. Materials and Methods

2.1. Ethical statements

The Helsinki Declaration and Institutional Research Ethics were followed to conduct the current study. gave their approval to this investigation. The Ethical Review Committee of the Chattagram, Maa-Shishu O General Hospital's ERB, provided the ethical clearance (Memo no. CMOSH/2020/1951). The consent form included the details of this study, research processes, voluntary participation, and their right to withdraw from the study at any time were all clearly described.

2.2. Study design

A retrospective cohort study design was utilized in the study. The comparative study was conducted between vaccinated and unvaccinated COVID-19 positive patients of the Chittagong Medical College Hospital, 250 Bed General Hospital, and Chattogram Maa-O-Shishu Hospital Medical College. A convenience sampling technique was implemented to recruit participants in the study from April to June 2021. Data were collected through personal interviews, and clinical investigations were received from the patient's follow-up datasheet. The inclusion criteria for the study were (i) being >18 years old, (ii) COVID-19 infected (patients tested COVID-19 positive by rRT-PCR test), (iii) vaccinated cohorts (took two doses of ChAdOx1 vaccine at least 28 days before the participation), (iv) unvaccinated cohorts (didn't uptake any kind of vaccine prior the participation in the

study), and (vi) Bangladeshi citizens. Individuals who were severely ill and did not provide consent to participate in the study were excluded.

2.3. Participant and procedure

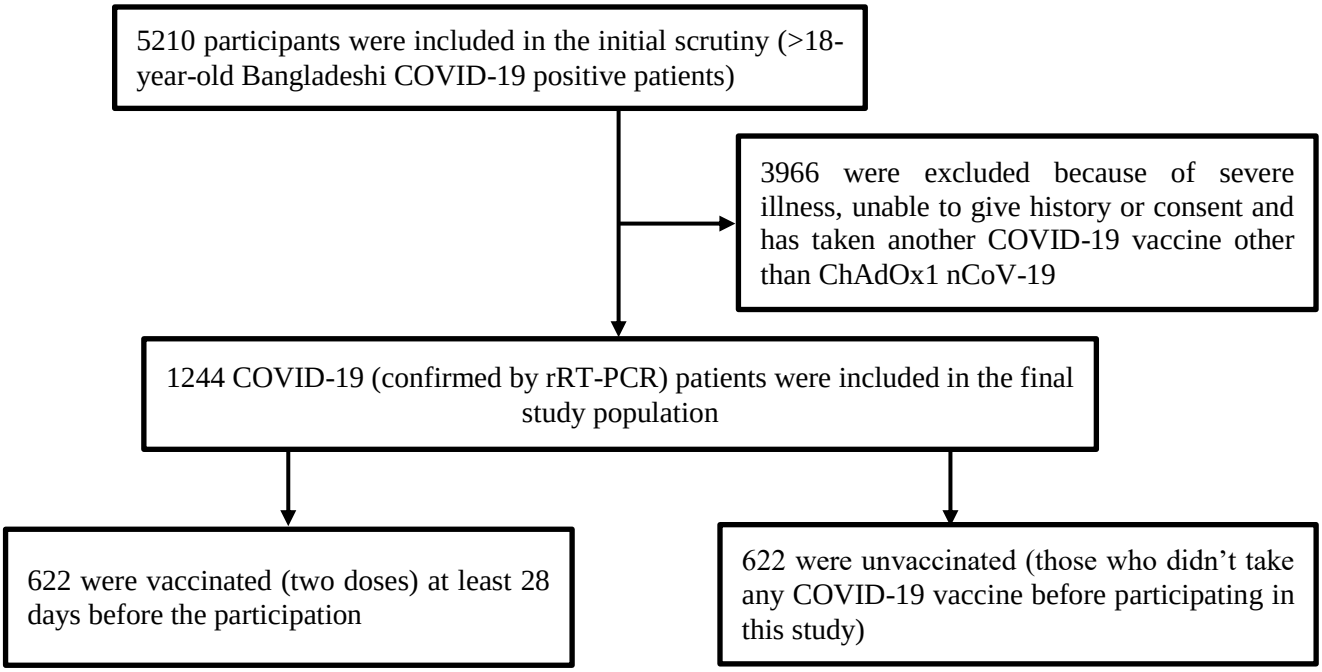

Figure 1. Flow-chart of the participants selection.

The COVID-19 diagnoses were made based on oropharyngeal and nasopharyngeal swab samples by real-time Reverse Transcription Polymerase Chain Reaction (rRT-PCR) in Chittagong Medical College Hospital, Chittagong 250 Bed General Hospital, and Chatagram Maa-O-Shishu Hospital Medical College in Bangladesh. We considered 1244 COVID-19 patients from the selected hospitals and divided them into two cluster groups vaccinated (622 people; those who took two doses of vaccine at least 28 days before the participation) and unvaccinated (622 people) (Figure 1). The present study evaluated the epidemiological characteristics regarding the vaccine status of the positive-tested COVID-19 patients. Patients visiting COVID-19 outdoor were initially questioned if they had gotten the vaccine and then tested for COVID-19 rRT-PCR. In addition, individuals admitted to the hospital directly were asked if they had received vaccines. All of these patients were followed up on until they were discharged or deceased. All data were obtained after the patients, or their guardians signed a written informed consent form. We also collected information from the follow-up sheet of the patients of the selected hospitals.

2.4. Variables selection

Socio-demographic questions were asked to obtain age, gender (male/female), residence (urban/rural) and occupation (job/business/housewife/health-worker). Smoking history was taken by 'yes/no' questions. Patient's conditions were also assessed by investigating oxygen therapy types [oxygen mask/high flow nasal cannula (HFNC)/non-invasive ventilation (NIV)/mechanical ventilation], the site of treatment [home care, COVID ward, high dependency unit (HDU), intensive care unit (ICU)], medications (Vitamins, Paracetamol, Antihistamine, Antiviral, Antiparasitic/Ivermectin, Azithromycin, Meropenem/Ceftriaxone, Steroid, Oral Anticoagulant, Enoxaparin, Tocilizumab, Plasma) and the presence of comorbidities (diabetic, hypertension, ischemic heart disease, chronic obstructive pulmonary disease, Bronchial Asthma, cancer, chronic kidney disease, intestinal lung disease, cardiovascular diseases, and chronic lung disease).

The questionnaire also included the presenting symptoms (asymptomatic, runny nose, lethargy/weakness, chest pain, body pain, fever, cough, shortness of breath, loss of smell, loss of taste, diarrhea has or not), severity (mild, moderate, severe, and critical) were noted. Biochemical and radiological investigations such as level of WBC (increased, decreased, normal, not tested), Platelet (normal, decreased, not tested), CRP (increased, normal, not tested), Ferritin (increased, normal, not tested), D-dimer (increased, normal, not tested), Chest X-ray P/A view (normal, not tested, bilateral consolidation, unilateral consolidation, not tested), chest high resolution

computed tomography (HRCT) (normal, not tested, ground-glass opacity) were also documented. Additionally, recovery time (we consider 7 to 35 days) from illness and death status are conjointly monitored.

2.5. Statistical analysis

Descriptive statistics have been measured for the prevalence of variables for vaccinated and unvaccinated patients. For the difference in the variables, the chi-squared test and Kruskal–Wallis test were examined (Flacco *et al*., 2021). The Cox proportional hazard model of survival analysis was used for two cohorts. For hazard ratio validation/assumption, Schoenfeld's test and the log-minus-log (LML) plot were used (Flacco *et al*., 2021). By the Cox proportional hazard model, we determine the hazard ratio. After calculating the hazard ratio controlling for unvaccinated, vaccine effectiveness was estimated as one minus hazard ratio, (1-HR) × 100 (Leval *et al*., 2016). Any five outcomes of the vaccinated and unvaccinated groups were considered for assessing vaccine effectiveness (Dagan *et al*., 2021). By the Log minus log (LML) curve, we determine the survival probability of a patient's improved status for time series (recovery time) by COVID-19 severity (mild, moderate, severe, and critical). The association of variables was considered statistically significant if the *P* value was less than 0.05. Data analysis was performed using the R programming language.

3. Results

3.1. Demographic characteristics

Among the vaccinated cohort, 37% (n=230) age was 50-59 years, 69% (430) were male, 76% (472) from the urban localities, 38% (236) were job holders/businessmen, 84% (522) were non-smoker, in terms of the treatment, 32% (200) were the oxygen mask users, 69% (430) got treatment at home without going hospital. 92% (572) patients took vitamins, and 88% (550) got paracetamol. In addition, 63% (390) had at least one comorbidity and 45% (278) were diabetic, 38% (238) hypertensive.

In the initial presentation, 81% (506) felt lethargy/weakness, and 66% (412) had mild disease severity. Among biochemical parameters, 66% (408) patients had raised WBC count with 36% increased lymphocyte, and 88% had normal platelet values. Alongside, 74% (462) had increased CRP, 49% (306) had normal ferritin level, and 48% (298) patients' D-dimer level was raised. Besides, 23% (142) patients had unilateral consolidation in chest X-ray (P/A view), and 66% (408) had normal chest HRCT. The mean (SD) of recovery time (days) was 14 (SD ± 7.18). The death of vaccinated patients was 3% (18), and 97% (604) were recovered after complete treatment.

In respect of the unvaccinated cohort, 39% (240) aged were in between 16-39 years, 62% (384) were male by sex, 59% (366) were living in the urban localities, 57% (352) were job holders/businessmen, 69% (432) were non-smoker, 29% (180) were oxygen mask user; 54% (336) took treatment at home instead of going hospital. In terms of treatment, among the non-vaccinated cohort, 96% (598) took vitamins, and 96% (598) took paracetamol. Apart from that, 24% (148) were diabetic patients, 23% (146) had hypertension, and 41% (258) had at least one comorbidity. In addition, 4% (24) were asymptomatic, 94% (582) had a fever, and 64% (398) had a cough initially (Table 1). Moreover, 56% (346) were suffering from the mild severity of the disease (Figure 2).

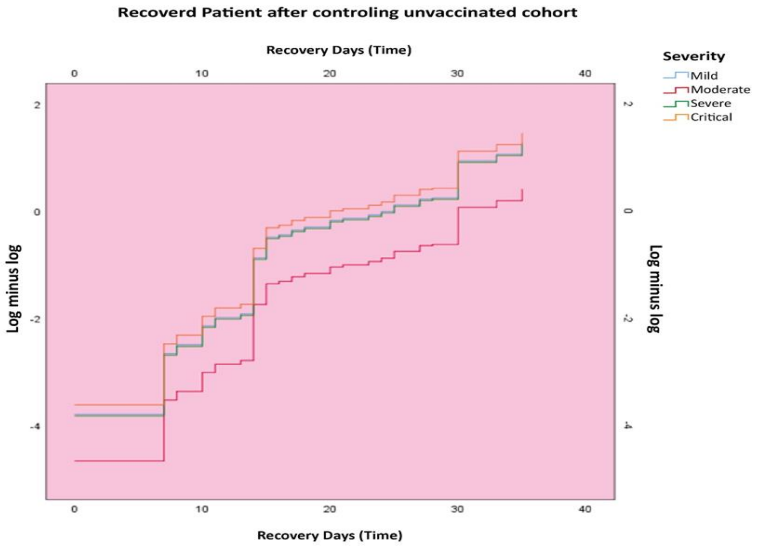

Figure 2. LML curve with Severity of COVID-19 Vaccine.

Table 1. Comparative presentation of demographic characteristics of vaccine status.

Variables		Vaccinated	Unvaccinated
Age (years)	16-39 years	90 (14%)	240 (39%)
	40-49 years	108 (17%)	134 (22%)
	50-59 years	230 (37%)	124 (20%)
	60-69 years	170 (27%)	82 (13%)
	70-79 years	24 (4%)	34 (5%)
	≥80years	0 (0%)	8 (1%)
Gender	Male	430 (69%)	384 (62%)
	Female	192 (31%)	238(38%)
Locality	Urban	472 (76%)	366(59%)
	Rural	150 (24%)	256(41%)
Occupation	Dependent	232 (37%)	130(21%)
	Job/business	236 (38%)	352(57%)
	Housewife	60 (10%)	100(16%)
	Health Worker	94 (15%)	40(6%)
Smoker	Yes	100 (16%)	190(31%)
	No	522 (84%)	432(69%)
Oxygen Therapy	Oxygen mask	200 (32%)	180(29%)
	HFNC	96 (15%)	50(8%)
	NIV	0 (0%)	24(4%)
	Mechanical ventilation	8 (1%)	94(15%)
Site of Treatment	Home Care	430 (69%)	336(54%)
	COVID ward	140 (23%)	274(44%)
	HDU	22 (4%)	98(16%)
	ICU	34 (5%)	50(8%)
Treatments	Vitamins	572 (92%)	598(96%)
	Paracetamol	550 (88%)	598(96%)
	Anti-histamine	316 (51%)	72(12%)
	Anti-viral	146 (23%)	224(36%)
	Anti-parasites/Ivermectin	344 (55%)	394(63%)
	Azithromycin	328 (53%)	246(40%)
	Meropenem/Ceftriaxone	200 (32%)	220(35%)
	Steroid	188 (30%)	204(33%)
	Oral Anticoagulant	68 (11%)	252(41%)
	Enoxaparin	206 (33%)	118(19%)
	Tocilizumab	28 (5%)	16(3%)
	Plasma	0 (0%)	62(10%)
Comorbidities	Diabetic	278 (45%)	148(24%)
	Hypertension	238 (38%)	146(23%)
	IHD	30 (5%)	0(0%)
	COPD	78 (13%)	34(5%)
	BA	18 (3%)	48(8%)
	Cancer	20 (3%)	4(1%)
	CKD	8 (1%)	22(4%)
	ILD	6 (1%)	2(0%)
	CVD	26 (4%)	8(1%)
	CLD	0 (0%)	4(1%)
Comorbidity	Yes	390 (63%)	258(41%)
	No	232 (37%)	364(59%)
Initial Presentations	Asymptomatic	30 (5%)	24(4%)
	Rhinorrhea	206 (33%)	172(28%)
	Insomnia	102 (16%)	6(1%)
	Lethargy/Weakness	506(81%)	56(9%)
	Chest pain	84(14%)	246(40%)
	Myalgia	214(34%)	260(42%)
	Fever	398(64%)	582(94%)
	Cough	402(65%)	398(64%)
	Dyspnea	88(14%)	130(21%)
	Anosmia	174(28%)	160(26%)

Table 1. Contd.

Variables		Vaccinated		Unvaccinated
Initial Presentations	Ageusia/Dysgeusia	154(25%)		144(23%)
	Diarrhea	74(12%)		68(11%)
Severity	Mild	412(66%)		346(56%)
	Moderate	172(28%)		128(21%)
	Severe	28(5%)		106(17%)
	Critical	10(2%)		42(7%)
Investigations	WBC	Increased	408(66%)	332(53%)
		Normal	142(23%)	158(25%)
		Not tested	70(11%)	132(21%)
	Platelet	Normal	550(88%)	490(79%)
		Not tested	70(11%)	132(21%)
	Lymphocyte	Decreased	162(26%)	232(37%)
		Increased	222(36%)	70(11%)
		Normal	168(27%)	188(30%)
		Not tested	70(11%)	132(21%)
	Neutrophil	Increased	218(35%)	168(27%)
		Normal	334(54%)	318(51%)
		Not tested	70(11%)	136(22%)
	CRP	Increased	462(74%)	324(52%)
		Normal	128(21%)	18(3%)
		Not tested	32(5%)	280(45%)
	Ferritin	Increased	232(37%)	226(36%)
		Normal	306(49%)	46(7%)
		Not tested	84(14%)	350(56%)
	D-dimer	Increased	298(48%)	230(37%)
		Normal	248(40%)	46(7%)
		Not tested	76(12%)	346(56%)
	Chest X-ray	Normal	0(0%)	6(1%)
		Not tested	420(68%)	252(41%)
		Bilateral Consolidation	60 (9.6%)	236 (38%)
		Unilateral Consolidation	142 (23%)	128 (21%)
	Chest HRCT	Normal	408 (66%)	12 (2%)
		Not tested	142 (23%)	364 (59%)
		Ground glass opacity	70 (11%)	246 (40%)
Recovery time (days)	Mean (SD)	14 (7.18)		16 (7.47)
R_X Outcome	Death	18 (3%)		78 (13%)
	Recovered	604 (97%)		544 (87%)

Among biochemical parameters, 53% (332) of patients' WBC was raised, 79% (490) had average platelet count, the lymphocyte count decreased in 37% (232) patients, and 51% (318) had a normal neutrophil level. Additionally, 52% (324) of patients' CRP was increased, 36% (226) had elevated ferritin levels, and 37% (230) had raised D-dimer levels. According to radiological findings, 38% (236) of patients showed bilateral consolidation on chest X-ray (P/A view), and 40% (246) had ground-glass opacity on chest HRCT. Recovery time (days) was 16 (7.47) on average (SD). At the end of the follow-up, 13% of unvaccinated patients died, whereas 87% (544) recovered (Table 1).

3.2. Vaccine effectiveness

Overall, 1244 patients with COVID-19 infection were included in this retrospective cohort study. Among them, 50% were unvaccinated, and 50% were vaccinated (ChAdOx1 nCoV-19). Compared with unvaccinated, the vaccine effectiveness can vary from 81% to 92% in respect of age. This vaccine was more effective among the 60-69 years old and can reduce 92% hazard of death [the HR ratio- 0.081 (.036-.179), *P*= 0.0001], and it also can reduce 46% hazard of death from the unvaccinated group [the HR ratio-0.541(0.456-0.642), *P*=0.0001] in the rural locality. Although gender and smoking habit did not show any significant association in regards to ChAdOx1 nCoV-19 vaccine effectiveness, they played a vital role in recovering the infections (Figure 3).

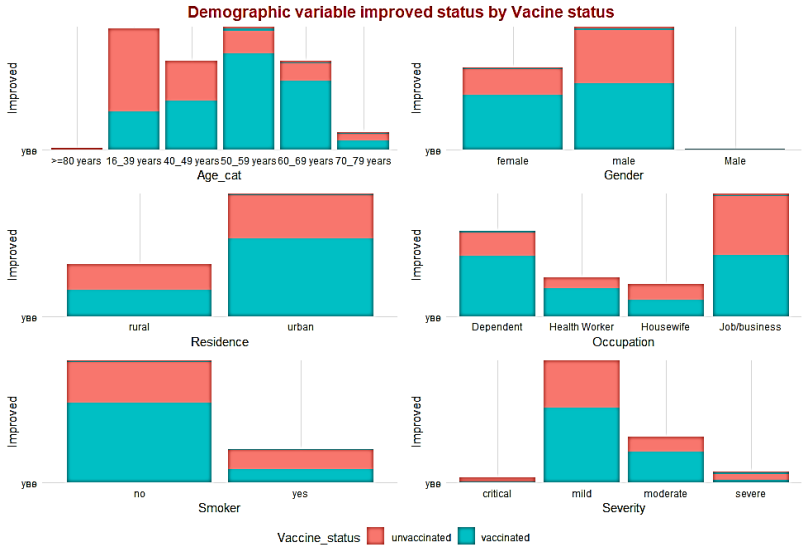

Figure 3. Vaccine status improvement for demographic variables.

Encompassed by treatment sites, home care was more effective for ChAdOx1 nCoV-19 vaccinated patients and can reduce 58% hazard of death [the HR ratio- 0.419 (0.224- 0.786), *P*=0.007]. Besides the initial presentations, asymptomatic patients with vaccination show more effectiveness against ChAdOx1 nCoV-19 can reduce 81% hazard of death [the HR ratio - 0.191(0.097- 0.373), *P*=0.0001] and moderate severity patients with vaccinated also can reduce 56% hazard of death [the HR ratio- 0.443(0.312- 0.629), *P*=0.0001]. LML curve also showed that moderate patients with hospital admission showed a higher level of vaccine effectiveness among other severity statuses. That means they recovered early (Figure 2). Among the investigation with vaccinated patients increased lymphocyte count [the HR ratio 0.591 (0.437- 0.800), *P*=0.001], normal CRP level [the HR ratio- 0.438(0.244- 0.788), P=0.006], increased ferritin level [the HR ratio- 0.428 (0.265- 0.690), P=0.0001] and increased D-dimer status [the HR ratio- 0.492 (0.325-0.778), *P*=0.004] showed benefits against this vaccine (Table 2).

Table 2. Hazard ratio of ChAdOx1 nCoV-19 vaccine among vaccinated vs. unvaccinated patients.

Variables		HR ratio (95% of CI)	P value	Vaccine Effectiveness, (%)
Age (years)	16-39 years	.259(.118-.569)	.001	84
	40-49 years	.106(.048-.236)	.0001	91
	50-59 years	.169(.077-.369)	.0001	83
	60-69 years	.081(.036-.179)	.0001	92
	70-79 years	.189(.080-.446)	.0001	81
	≥80 years	1	1	NA
Gender	Male	1.155(.871-1.533)	.317	0
	Female	1	1	NA
Locality	Urban	.541(.456-.642)	.0001	46
	Rural	1	1	NA
Occupation	Dependent	1.452(.983-2.147)	.061	0
	Job/business	2.820(1.959-4.058)	.0001	0
	Housewife	3.583(2.400-5.350)	.0001	0
	Health Worker	1	1	NA
Smoker*	Yes	1.062(.860-1.311)	.578	0
Oxygen Therapy*	Oxygen mask	1.844(1.533-2.220)	.0001	0
	HFNC	1.716(1.272-2.316)	.0001	0
	NIV	.820(.535-1.257)	.363	18
	Mechanical ventilation	.361(.287-.453)	.0001	64
Site of Treatment*	Home Care	.419(.224-.786)	.007	58
	COVID ward	.581(.315-1.070)	.0081	42
	HDU	.753(.543-1.044)	.0089	25
	ICU	1.144(.776-1.685)	.496	0

Table 2. Contd.

Variables			HR ratio (95% of CI)	P value	Vaccine Effectiveness, (%)
Treatments*	Vitamins		1.309(.837-2.049)	.238	0
	Paracetamol		1.148(.732-1.800)	.549	0
	Anti-histamine		4.211(3.220-5.506)	.0001	0
	Anti-viral		.743(.584-.946)	.016	26
	Anti-parasites/Ivermectin		.882(.716-1.086)	.236	18
	Azithromycin		1.054(.862-1.288)	.608	0
	Meropenem/Ceftriaxone		1.289(.973-1.708)	.077	0
	Steroid		1.709(1.320-2.213)	.0001	0
	Oral Anticoagulant		.650(.513-.824)	.0001	35
	Enoxaparin		1.661(1.277-2.162)	.0001	0
	Tocilizumab		.471(.271-.819)	.008	53
	Plasma		.164(.115-.234)	.0001	84
Comorbidities*	Diabetic		.366 (.268-.499)	.0001	63
	HYPERTENSION		.534(.399-.715)	.0001	47
	IHD		.009(.000-4.925)	.0489	91
	COPD		.709(.466-1.080)	.109	29
	BA		.911(.653-1.271)	.583	9
	CANCER		.497(.153-1.618)	.0246	50
	CKD		2.108(1.327-3.350)	.002	0
	ILD		1.302(.237-7.155)	.762	0
	CVD		.791(.363-1.726)	.0456	21
	CLD		1.639(.519-5.175)	.400	0
Initial Presentations*	Asymptomatic		.191(.097-.373)	.0001	81
	Rhinorrhea		1.467(1.097-1.960)	.010	0
	Insomnia		3.007(1.276-7.090)	.012	0
	Lethargy/Weakness		5.423(4.005-7.344)	.0001	0
	Chest pain		.759(.641-.898)	.001	24
	Myalgia		.613(.516-.730)	.0001	39
	Fever		.345(.206-.580)	.0001	66
	Cough		1.122(.927-1.357)	.237	0
	Dyspnea		.978(.791-1.209)	.837	2
	Anosmia		1.022(.840-1.242)	.830	0
	Ageusia/Dysgeusia		1.184(.959-1.463)	.116	0
	Diarrhea		.699(.556-.880)	.002	30
Severity	Mild		.891(.643-1.235)	.048	11
	Moderate		.443(.312-.629)	.0001	56
	Severe		1.568(1.094-2.245)	.014	0
	Critical		1	1	NA
Investigations	WBC	Decreased	1.337(.472-3.788)	.585	0
		Increased	2.586(.904-7.398)	.076	0
		Normal	1	1	NA
	Lymphocyte	Decreased	2.453(1.771-3.396)	.0001	0
		Increased	.591(.437-.800)	.001	41
		Normal	1	1	NA
	Neutrophil	Increased	.469(.173-1.273)	.137	0
		Normal	.764(.279-2.090)	.600	0
		Not tested	1	1	NA
	CRP	Increased	.698(.511-.955)	.024	30
		Normal	.438(.244-.788)	.006	57
		Not tested	1	1	NA
	Ferritin	Increased	.428(.265-.690)	.0001	58
		Normal	.0001(.000-.52)	.692	99
		Not tested	1	1	NA
	D-dimer	Increased	.492(.325-.778)	.004	51
		Normal	.0001(.000-.52)	.765	99
		Not tested	1	1	NA

"No" indicate as reference categories.

4. Discussion

The vaccine is one of biomedical science's most significant successes and effective public health interventions of the twentieth century (CDC, 1999). Vaccinations have saved millions of people from different infectious diseases, hospitalizations, and deaths worldwide (Mawson *et al*., 2017). The present study provided preliminary real-world evidence for the effectiveness of the Oxford-AstraZeneca ChAdOx1nCoV-19 vaccine against COVID-19-infected individuals, hospital admissions, severity, and death in older adults in Bangladesh. To the best of the authors' knowledge, this is the first large-scale comparative retrospective cohort study among vaccinated and unvaccinated COVID-19 infected patients assessing the effectiveness of the ChAdOx1 nCoV-19 Vaccine.

However, this study found that the ChAdOx1 nCoV-19 vaccine could be 81%-92% effective for its receivers by reducing, i) the risk of getting and spreading the virus, ii) severity of COVID-19-related illness and death, and iii) hospital admission. Moreover, it could reduce 69% of hospital admission. The study also showed that 97% of vaccinated patients recovered without major complications compared to unvaccinated cohorts. In addition, the study also revealed the ChAdOx1 nCoV-19 Vaccine was most effective for individuals 60-69 years of age. The vaccine also showed safety and efficacy for comorbid patients. Moreover, it could reduce 64% of mechanical ventilation necessity. The study found no association between gender, occupation, and smoking habit with vaccine effectiveness. Several studies conducted internationally support our findings.

Though in this study, we only evaluated the effectiveness of the ChAdOx1 nCoV-19 vaccine by comparing vaccinated and unvaccinated cohorts. Demonstrating these vaccines, the timing between the first and second dose can vary (i.e., 21 days for Pfizer–BioNTech and 28 days for ChAdOx1 nCoV-19) (Flacco *et al*., 2021; Sheikh *et al*., 2021). The average timing of two doses of ChAdOx1 nCoV-19 vaccine was 60 days in Bangladesh and showed high effectiveness towards COVID-19. The recommended date of the first dose of ChAdOx1 nCoV-19 was 8-12 weeks, but studies showed that the immunity had grown stronger after six months of the first dose (Voyssey *et al.,* 2021). The combination of two different COVID-19 vaccines gives protection against all variants (Voysey *et al.,* 2021).

Moreover, our study found the effectiveness of the ChAdOx1 nCoV-19 vaccine was 81%- 92%.. However, the effectiveness was different for the different age groups. This difference may be due to the influence or impact of age on the effectiveness of the vaccine. Nonetheless, a population-based study showed that age influences the effectiveness of the vaccine (Cerqueira-Silva *et al.*, 2022). In addition, a meta-analysis study also showed that the age difference has an impact on the efficacy and safety of the COVID-19 vaccines (Wang *et al.,* 2021). Furthermore, our finding aligns with another study conducted among hospitalized patients in England and found two doses of the ChAdOx1 nCoV-19 vaccine can be effective, and it could also work against the Alpha variant (Stowe *et al.,* 2021). A meta-analysis study showed that a complete dose of this vaccine provides 84% effectiveness (Rahmani *et al.*, 2021). Another study conducted in England among older adults found that a single ChAdOx1 nCoV-19 vaccine was about 60-75% effective (Bernal *et al.,* 2021). Additionally, a study from Sweden, showed that the ChAdOx1 nCoV-19/mRNA vaccine was 79% effective (Nordström *et al.,* 2021). Consequently, elderly people may take 28 days after a single ChAdOx1 nCoV-19 dose, which can neutralize the antibody with an adjusted 80.4% effectiveness (Hyams *et al.*, 2021). For the older age with symptomatic COVID-19 infection, and for the mass population or outdoor patients' vaccine effectiveness can vary from 47%-70% for 1st dose and 85%-96% for 2nd doses *(*Mahase, 2021; Chodick *et al.,* 2021; Dagan *et al.,* 2021; Haas *et al.,* 2021). However, the effectiveness could vary in terms of age, country, immune systems, and other factors associated with health.

Although, the COVID-19 vaccines are still expected to be effective at preventing severe disease, hospitalization, and death. However, according to our study ChAdOx1 nCoV-19 vaccine was 46% more effective for rural participants compared to urban. Though, **s**everal vaccine studies also elicit lower efficacy or impaired immune responses in rural participants compared to urban settings in a low-income country (Dagan *et al.,* 2021).

In addition, our findings showed that vaccinated cohorts needed less hospitalization compared with unvaccinated cohorts. Our study found that the vaccine could reduce 58% of hospital admission for vaccinated people with 60 days interval of two doses of the ChAdOx1 nCoV-19 vaccine. Aligning with our findings, a couple of studies stated that the vaccines could prevent COVID-19–associated hospitalizations *(*Moline *et al.*, 2021*)*, reduce the discharge of subsequent infection, morbidity, and mortality (Hoe *et al*., 2021), in older adults, and 88% effective after 28–34 days of vaccination (Vasileiou *et al.,* 2021). A meta-analysis study showed that the full dose of the vaccine could reduce 56% of hospital admission, the BNT162b2 mRNA vaccine reduced 73% (Rahmani *et al.,* 2021), and the Gam-COVID-Vac (Sputnik) vaccine prevents 87.6% of hospitalization (González *et al.,* 2021). Moreover, the AstraZeneca vaccine was found to be 92% and 86% effective in

preventing hospitalization owing to the Delta and Alpha strains, respectively, and there were no deaths among individuals who were vaccinated in Bangladesh (Stowe *et al.,* 2021).

Moreover, the ChAdOx1 nCoV-19/mRNA vaccine was also effective for comorbid patients. Our study showed that this vaccine was 91% effective for ischemic heart disease patients and 63% for diabetic patients. A multi-country randomized control trials study of the ChAdOx1 nCoV-19 vaccine also showed that this vaccine was safe and effective for comorbid patients (Voysey *et al.,* 2021). The clinical trial of the ChAdOx1 nCoV-19 vaccine in Brazil showed that people with comorbidities (cardiovascular disease, lung disease, Diabetes Mellitus, etc.) had slightly lower efficacy (58.3%) than other people (Choi and Cheong, 2021*).* But we found moderate to higher effectiveness in our study for mass vaccination with these comorbidities. Additionally, one single dose of this vaccine among elderly and comorbid patients could reduce the risk of infection (Public Health Ontario, 2021). However, a recent study found that the vaccine could be effective 76.7% for the adjusted variable with one dose and 80.4% for the unadjusted variable with a one-dose vaccine (Choi and Cheong, 2021), safety, and efficacy.

However, for some countries, the effectiveness of vaccine could be associated with different factors such as one dose giving moderate protection and the second dose providing satisfactory protection (Campbell *et al*., 2021; Duff Putu *et al.,* 2016). Another study suggested that most recently used vaccines were less immunogenic and effective in the elderly compared to younger adults (Ciabattini *et al.,* 2018; Duff Putu *et al.,* 2016). For getting the actual effectiveness, the vaccine should be added to the other treatment options for proper management of COVID-19 (Noor, 2021). The COVID-19 vaccination could minimize infection in both asymptomatic and symptomatic patients (Harder *et al.,* 2021). Although efficacy might not be condensed, a safe and effective vaccine is needed to control this pandemic; it is essential to investigate the vaccine's efficacy against every variant (Emary *et al.,* 2021; Kabagenyi *et al.,* 2020). The effectiveness against the Beta variant was moderately low, and this transmissibility of the variant of concern causes a risk of high to very high for the general people and very high for susceptible individual. In addition, our study found, that the ChAdOx1 nCoV-19 vaccine had higher effectiveness (56%) for moderately severe COVID-19 patients, and in the US, the study also showed that moderate COVID-19 patients could reduce 76% hazard of death (Kabagenyi *et al.,* 2020; Moline *et al.,* 2021). According to WHO, the ChAdOx1 nCoV-19 vaccine seemed to have lower efficacy than the Pfizer vaccine at preventing mild to moderate patients (Moline *et al.,* 2021; WHO, 2021b). However, as there were no certain evidence that vaccinated people couldn't transmit the COVID-19; thus, following public health precaution measures would be more beneficial such as using masks, maintaining physical distance, and handwashing (WHO, 2021b).

However, to date, there is scarce evidence regarding the effectiveness of the ChAdOx1 nCoV-19 vaccine from Bangladesh. Moreover, as the provided vaccine was made in India (Serum Institute of India) and as there were differences among population characteristics, therefore a study regarding the effectiveness of this vaccine is needed and the present study is carried out to generate some baseline evidence to compile recommendations for the future study.

5. Conclusions

The study found the ChAdOx1 nCoV-19 Vaccine is highly effective for receivers. The vaccinated cohorts showed much immunity against the virus, and the infection, severity, and hospital admission rate were much fewer than the unvaccinated cohorts. The study may also help to guide policymakers to provide mass vaccinations more rapidly to pause the COVID-19 pandemic. The findings also suggest that vaccines are highly effective for people with underlying medical conditions, so these groups of people should cover vaccination on a priority basis. In addition, herd immunity, which is achieved through mass vaccination, will provide the best indirect protection for vulnerable people.

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Data availability

The datasets obtained for this study are accessible to the corresponding author upon reasonable request.

Conflict of interest

None to declare.

Authors' contributions

Conceptualization: SD, MSHS. Data Collection, validation, and manuscript writing: SD, RKR, MSHS, NIT, AAK, AD, RSRB, MMH, SR, MA and MMH. Analysis and interpretation of data: RKR, and MSHS. Editing and critical revision of the manuscript: KNK, and MSHS. All authors have read and approved the manuscript.

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