Original Article

The Effectiveness of SARS-CoV-2 Vaccination in Preventing Severe Illness and Death – Real-world Data from a Cohort of Patients Hospitalized with COVID-19

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Abstract

Background: While long-term studies on the correlates of protection, vaccine effectiveness, and enhanced surveillance are awaited for SARS-CoV-2 vaccine, studies on breakthrough infections help understand the nature and course of this illness among vaccinated individuals and guide in public health preparedness. This study aims to compare the differences in the hospitalization outcomes SARS-CoV-2 infection of fully vaccinated individuals with with those of unvaccinated and partially vaccinated individuals. **Materials and Methods:** Single institution observational cohort study. This study compared the differences in clinical, biochemical parameters and the hospitalization outcomes of 53 fully vaccinated individuals with those of unvaccinated (1464) and partially vaccinated (231) individuals, among a cohort of 2,080 individuals hospitalized with SARS-CoV-2 infection. Descriptive statistics and propensity-score weighted multivariate logistic regression analysis adjusting for clinical and laboratory parameters were used to compare the differences and to identify factors associated with outcomes. **Results:** Completing the course of vaccination protected individuals from developing severe COVID-19 as evidenced by lower proportions of those with hypoxia, abnormal levels of inflammatory markers, requiring ventilatory support, and death compared to unvaccinated and partially vaccinated individuals. There were no differences in these outcomes among patients who received either vaccine type approved in India. **Conclusions:** Efforts should be made to improve the vaccination rates as a timely measure to prepare for the upcoming waves of this highly transmissible pandemic. Vaccination rates of the communities may also guide in the planning of the health needs and appropriate use of medical resources.

Keywords: Breakthrough infection, mortality, SARS-CoV-2 vaccine, severe illness

Introduction

Two COVID-19 vaccines, Covaxin (whole-virion SARS-CoV-2 vaccine strain NIV-2020-770) and Covishield (recombinant replication-deficient chimpanzee adenovirus vector encoding the spike protein ChAdOx1 nCoV-19) have been given emergency use authorization by the Indian regulatory authority and have been rolled out on a mass scale. An interim analysis of four randomized control trials (RCTs) of Covishield vs control has reported an overall efficacy of 70·4% among 11,636 participants.[1] Recent RCT of Covaxin vs placebo on 25,798 individuals in India reported vaccine efficacy of 93.4% against severe COVID-19 and 63% against asymptomatic COVID-19, with an overall vaccine efficacy of 77.8%.[2] However, randomized trials may not reflect the real-world data. Moreover, due to the nature of the pandemic, vaccine trials had a short duration of follow-up before they were authorized for public use.[3-5]

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In order to better understand the level of protection offered by the vaccines, it is essential to study the effectiveness of the vaccine pragmatically. Until data from such long-term prospective studies on vaccinated cohorts are available, examining rates of asymptomatic and severe infections, requirement for hospitalization, oxygen or ventilatory support, etc., among breakthrough infections offer a window of opportunity to estimate vaccine effectiveness amongst vaccinated individuals. Reports of breakthrough infections from India till data are mostly limited to health care workers of single institutions and with no comparisons of the inflammatory response or course of illness during the hospital stay.[6-12] Our study aims to compare the differences in clinical and biochemical parameters and the hospitalization outcomes of fully vaccinated individuals with SARS-CoV-2 infection with those of unvaccinated and partially vaccinated individuals.

Methods

The study cohort included patients admitted to our COVID-19 treatment facility from April 2021 to June 2021. The protocol was designed keeping in mind the STROBE checklist for observational studies and was approved by the institutional review board. We classified the patients into three groups based on the duration of having the symptoms from the date of vaccination:

- *Unvaccinated*: Those who had not received any vaccine or became symptomatic in <2 weeks of receiving the first dose
- *Partially vaccinated*: Got symptomatic two or more weeks after the first dose but not received the second dose or received the second dose <2 weeks before getting symptomatic
- *Fully vaccinated*: Participants who became symptomatic two or more weeks after the receipt of the second dose of the vaccine.

Patients were classified into mild, moderate, and severe COVID-19 according to the NIH recommendations.[13] Clinical symptoms, baseline laboratory parameters, treatments offered, and complications during hospital stay were collected from the case files and electronic hospital records. The outcomes of the patients considered for analysis were– development of severe illness needing oxygen therapy, deterioration in clinical condition during hospital stay, and death. Description of the entire sample cohort, methodology of data collection, and definition of the study variables are described in detail elsewhere.[14]

Statistical analysis

Propensity-score weighting with age, gender, and comorbidities was done to remove baseline imbalances between the vaccinated and unvaccinated groups since patients who were older than 60 years and those with co-morbidities were initially offered the vaccine. Propensity-score weighted univariate and multivariate logistic regression analysis adjusting for various clinical and laboratory parameters was done to compare the odds of occurrence of various events (such as oxygen requirement, ventilatory support, critical illness, and death) by vaccination status and survival curves were plotted for each study group.

Results

Of the 1,748 individuals ≥18 years and above which constituted our analysis cohort, 71.4% (1248) had not received any dose of the vaccine. 23.0% (402) had received one dose of the vaccine while 5·6% (98) received both doses of the vaccine. Based on the vaccination status classification described above in the methodology, we had 1,464 unvaccinated patients (1,248 who never received any dose of vaccine and 216 who had symptoms within 14 days of receiving the 1st dose), 231 partially vaccinated patients (186 individuals who received 1st dose of vaccine and developed symptoms >14 days from the date of vaccination and those who received both the doses of the vaccine but developed symptoms within 14 days of receiving the 2nd dose.) and 53 completely vaccinated individuals (who developed symptoms of COVID-19 after 14 days of receipt of the 2nd dose) who were considered as breakthrough infections. Table 1 shows the demographic and baseline clinical characteristics of the cohort.

Table 2 compares the proportions of individuals with abnormal lab parameters and inflammatory markers by vaccination status. Proportions of those with high d-Dimer, interleukin 6 (IL-6), ferritin, and C-reactive protein (CRP) were significantly low in the breakthrough infection group compared to others. Median values of total leukocyte counts; absolute neutrophil counts; liver function tests such as aspartate transaminase, alanine transaminase, alkaline phosphatase, and lactate dehydrogenase; and serum urea were significantly lower in the breakthrough infection group compared to others [Supplementary Table 1]. Significant differences also existed among these parameters between unvaccinated and partially vaccinated groups and even between the partially vaccinated and fully vaccinated groups.

Table 3 describes the treatments and interventions received by the individuals in the study cohort during their period of hospitalization, complications developed during the hospital stay, and their outcome. A significantly lesser proportion of the individuals with breakthrough infection required oxygen supplementation (18·2%) or ventilatory support (5.0%) compared to the individuals in the other groups. Very few of these individuals deteriorated (9·1%) or ever progressed to critical illness (4·6%) during their hospital stay compared to other study groups. The need for use of steroids, doxycycline, and anti-viral agents such as remdesivir was also significantly low in the breakthrough infection group. Only 3.9% in the breakthrough infection group developed renal dysfunction while a significantly higher proportion of those in the unvaccinated and partially vaccinated groups developed renal dysfunction (19.4% and 21.3% respectively) during illness.

Three individuals (5.7%) out of the 53 who developed breakthrough infection succumbed to illness while the case

Table 1: Demographic and baseline clinical profile of study cohort

	Vaccination status (*n*=1748)			
	Unvaccinated (1464; 83.8%), *n* (col%)	Partially vaccinated (231; 13.2%), *n* (col%)	Fully vaccinated (53; 3.0%), *n* (col%)	*P*
Age (years)				
18-44	607 (41.5)	55 (23.8)	28 (52.83)	<0.001
45-60	514 (35.1)	81 (35.1)	14 (26.42)	
>60	343 (23.4)	95 (41.1)	11 (20.75)	
Male gender	953 (65.1)	156 (67.5)	39 (73.58)	0.360
Comorbidities	*n*=1455	*n*=219	*n*=47	
No comorbidity	742 (51.0)	88 (40.2)	31 (65.96)	
1 comorbidity	448 (30.8)	76 (34.7)	9 (19.15)	0.004
≥2 comorbidities	265 (18.2)	55 (25.1)	7 (14.89)	
Hypertension	329 (22.6)	80 (36.5)	8 (17.02)	<0.001
Diabetes	317 (21.8)	75 (34.3)	7 (14.89)	<0.002
CAD	65 (4.5)	18 (8.2)	2 (4.26)	0.066
Neurological	24 (1.7)	1 (0.5)	0	0.391
CLD	4 (0.3)	0	0	0.693
Malignancy	70 (4.8)	3 (1.4)	0	0.017
Asthma/COPD	40 (2.8)	6 (2.7)	4 (8.51)	0.093
Hematological	7 (0.5)	0	0	0.674
CKD	16 (1.1)	3 (1.4)	0	0.840
Hypothyroidism	72 (5.0)	8 (3.7)	3 (6.38)	0.544
Clinical presentation at baseline	*n*=1464	*n*=228	*n*=53	
Asymptomatic	77 (5.3)	12 (5.3)	8 (15.1)	0.009
Symptomatic	1387 (94.7)	216 (94.8)	45 (84.91)	
Symptom distribution	*n*=1365	*n*=196	*n*=38	
Fever	1109 (81.3)	159 (81.2)	31 (81.6)	0.998
Dry cough	770 (56.4)	111 (56.6)	24 (63.2)	0.710
Cough with expectoration	184 (13.5)	18 (9.2)	3 (7.9)	0·159
Breathlessness	762 (55.8)	101 (51.5)	10 (26.3)	0.001
Rhinitis	52 (3.8)	13 (6.6)	5 (13.2)	0·008
Sore throat	266 (19.5)	48 (24.5)	12 (31.6)	0.059
Fatigue	248 (18.7)	30 (15.3)	12 (31.6)	0.058
Myalgia	277 (20.3)	41 (20.9)	8 (21.1)	0.974
Chest pain	115 (8.4)	12 (6.1)	7 (18.4)	0.051
Gastrointestinal symptoms	173 (12.7)	24 (12.2)	6 (15.8)	0.833
Drowsiness	12 (0.9)	3 (1.5)	1 (2.6)	0.194
Loss of smell	128 (9.4)	12 (6.1)	4 (10.5)	0.278
Loss of taste	124 (9.1)	16 (8.2)	5 (13.2)	0.545
Tachypnea (RR ≥24/min)	261 (19.1)	41 (20.9)	1 (2.6)	0.007
Oxygen status at admission	*n*=1435	*n*=209	*n*=44	
Room air	1102 (76.8)	169 (80.9)	40 (90.91)	0.037
Oxygen	333 (23.2)	40 (19.4)	4 (9.09)	
Baseline severity	*n*=1464	*n*=231	*n*=53	
Asymptomatic - No hypoxia	68 (4.6)	11 (4.6)	7 (13.2)	<0.001
Mild	452 (30.9)	74 (32.0)	27 (50.9)	
Moderate	204 (13.9)	30 (13.0)	3 (5.7)	
Severe (SpO_2 <94%)	710 (48.5)	93 (40.3)	7 (13.2)	

CAD: Coronary artery disease, CKD: Chronic kidney disease, COPD: Chronic obstructive pulmonary disease, CLD: Chronic liver disease, RR: Respiratory rate, SpO_2: Oxygen saturation

fatality rate was significantly higher in the unvaccinated (22.8%) and partially vaccinated (19.5%) groups. The temporal trend of symptom onset from the date of 1st dose vaccine receipt among those who received only one dose of vaccine are depicted in Figure 1. Majority of the patients who received only the first dose of vaccine presented with symptom onset within 2 weeks of receipt of the dose. Table 4 shows the results of the propensity score weighted logistic regression models and odds for various hospitalization outcomes across the study groups. After adjusting for baseline severity of the disease and

Table 2: Laboratory parameters of the study cohort at baseline

Categorical	Unvaccinated		Partially vaccinated		Fully vaccinated		*P*
	Tested (*n*)	Abnormal, *n* (%)	Tested (*n*)	Abnormal, *n* (%)	Tested (*n*)	Abnormal, *n* (%)	
Hemoglobin (<11 mg/dl)	1221	212 (17.4)	188	28 (14.9)	42	1 (2.4)	0.015
Thrombocytopenia (<1.5 lac/mm^3)	1224	247 (20.4)	189	35 (18.5)	44	12 (27.3)	0.412
White blood cell count	1217		188		42		
Leucopenia (<4000/mm^3)		154 (12.7)		16 (8.5)		6 (14.3)	0.038
Leukocytosis (>11,000/mm^3)		344 (28.3)		47 (25.0)		5 (11.9)	
LDH (>246 U/L)	1058	865 (81.8)	158	113 (71.5)	40	14 (35.0)	<0.001
Total bilirubin (>1.2 mg/dl)	1239	64 (5.2)	190	9 (4.7)	44	1 (2.3)	0.887
ALT (≥34 U/L)	1228	608 (49.5)	189	78 (41.3)	44	10 (22.7)	<0.001
AST (≥49 U/L)	1228	894 (72.8)	189	114 (60.3)	44	21 (47.7)	<0.001
Urea (≥50 mg/dl)	1246	355 (28.5)	189	57 (30.2)	45	3 (6.7)	0.002
Creatinine (≥1.0 mg/dl)	1245	223 (17.9)	190	36 (19.0)	45	4 (8.9)	0.281
Hyperferritinemia (>322 ng/mL)	440	279 (63.4)	65	34 (52.3)	14	6 (42.9)	0.071
D-dimer (>500 ng/ml)	1042	272 (26.1)	165	40 (24.2)	42	3 (7.1)	0.011
IL-6 (>4.4 pg/ml)	592	471 (79.6)	87	55 (63.2)	13	6 (46.2)	<0.001
CRP (>0.5 mg/dl)	1166	997 (85.5)	181	144 (79.6)	44	26 (59.1)	<0.001

ALT: Alanine transaminase, AST: Aspartate transaminase, CRP: C-reactive protein, IL-6: Interleukin-6, LDH: Lactate dehydrogenase

Table 3: Treatment patterns and in-hospital complications

Variable	Vaccination status (*n*=1748)						
	Unvaccinated		Partially vaccinated		Fully vaccinated		*P*
	Data available (*n*)	*n* (col%)	Data available (*n*)	*n* (col%)	Data available (*n*)	*n* (col%)	
Respiratory support	1425	874 (61.33)	211	116 (54.98)	44	8 (18.18)	<0.001
High flow nasal cannula	1407	113 (8.03)	211	12 (5.69)	44	1 (2.27)	0.239
Noninvasive ventilation	1420	212 (14.93)	211	30 (14.22)	44	0	0.005
Invasive mechanical ventilation	1424	205 (14.4)	211	23 (10.9)	44	2 (4.55)	0.075
Deteriorated during hospital stay	1427	507 (35.53)	211	72 (34.12)	44	4 (9.09)	<0.001
Critical illness	1448	288 (20.17)	211	39 (18.48)	44	2 (4.55)	0.019
Treatments received							
Steroids	1418	893 (62.98)	210	124 (59.05)	44	11 (25)	<0.001
Ivermectin	1379	235 (17.04)	202	33 (16.34)	44	5 (11.36)	0.685
Doxycycline	1378	272 (19.74)	203	35 (17.24)	44	2 (4.55)	<0.001
Minocycline	1378	33 (2.39)	203	3 (1.48)	44	0	0.647
Azithromycin	1376	206 (14.97)	203	20 (9.85)	44	3 (6.82)	0.063
Ceftriaxone	1378	222 (16.11)	203	30 (14.78)	44	8 (18.18)	0.805
Levofloxacin	1380	187 (13.55)	203	28 (13.79)	44	4 (9.09)	0.755
Tocilizumab	1377	31 (2.25)	199	2 (1.01)	44	1 (2.27)	0.512
Remdesivir	1375	333 (24.22)	201	34 (16.92)	44	5 (11.36)	0.012
Zinc supplements	1330	376 (28.27)	192	63 (32.81)	42	10 (23.81)	0.334
In Hospital complications							
Hyperglycemia	1302	323 (24.81)	188	52 (27.66)	43	5 (11.63)	0.079
Renal dysfunction	1340	260 (19.4)	207	44 (21.26)	51	2 (3.92)	0.007
Hypotension	1411	77 (5.46)	206	10 (4.85)	44	1 (2.27)	0.836
Outcomes							
Discharge		1130 (77.19)		186 (80.52)		50 (94.34)	0.004
Death		334 (22.81)		45 (19.48)		3 (5.66)	

time to presentation (Model-3, Table 4), individuals who had breakthrough infection had lesser odds of requiring oxygen support and deteriorating during hospital stay compared to the unvaccinated group, but the odds of developing critical illness and dying no longer differed by vaccination status. And when adjusted for laboratory parameters and inflammatory markers as well [Model-4, Table 4], the odds of having various outcomes did not differ across the study groups.

Sensitivity analysis using the number of doses of vaccine received irrespective of the vaccine protection status within

Table 4: Propensity score weighted logistic regression models assessing the odds of various outcomes

Reference: Unvaccinated	Model-1	Model-2	Model-3	Model-4
Oxygen requirement				
Partially vaccinated	0.77 (0.57-1.03),0.082	0.57 (0.42-0.78), <0.001	0.61 (0.36-1.06), 0.078	0.53 (0.28-1.01), 0.054
Fully vaccinated	0.44 (0.07-0.31), <0.001	0.14 (0.07-0.31), <0.001	0.24 (0.06-0.95), 0.042	0.33 (0.08-1.35), 0.123
Ventilatory support				
Partially vaccinated	0.89 (0.61-1.31), 0.565	0.71 (0.48-1.05), 0.087	0.73 (0.46-1.16), 0.179	0.78 (0.45-1.35), 0.379
Fully vaccinated	0.21 (0.05-0.86), 0.030	0.23 (0.06-0.94), 0.041	0.49 (0.09-2.53), 0.392	0.81 (0.07-8.78), 0.860
Deterioration during hospital stay				
Partially vaccinated	0.94 (0.69-1.28), 0.680	0.75 (0.55-1.04), 0.086	0.73 (0.51-1.04), 0.079	0.72 (0.46-1.14), 0.159
Fully vaccinated	0.18 (0.07-0.52), 0.001	0.20 (0.07-0.53), 0.001	0.28 (0.10-0.81), 0.019	0.50 (0.15-1.73), 0.277
Critical illness				
Partially vaccinated	0.90 (0.62-1.31), 0.571	0.71 (0.48-1.05), 0.087	0.71 (0.45-1.11), 0.134	0.78 (0.46-1.34), 0.367
Fully vaccinated	0.19 (0.05-0.81), 0.025	0.22 (0.05-0.90), 0.036	0.46 (0.09-2.37), 0.353	0.83 (0.07-9.87), 0.881
Death				
Partially vaccinated	0.84 (0.59-1.19), 0.325	0.65 (0.45-0.94), 0.020	0.64 (0.41-1.00), 0.051	0.67 (0.38-1.19), 0.171
Fully vaccinated	0.21 (0.07-0.68), 0.009	0.25 (0.08-0.79), 0.018	0.57 (0.16-2.06), 0.388	1.68 (0.35-8.07), 0.514

Propensity score weighted logistic regression models. Model 1: Univariate, Model 2: Adjusted for age, sex and comorbidities, Model 3: Model 2 plus adjusting for symptoms and symptom onset, Model 4: Model 3 plus adjusting for baseline lab parameters. Deterioration: No hypoxia at presentation, but developed hypoxia during stay, Critical illness: Required ventilatory support and/or developed hypotension

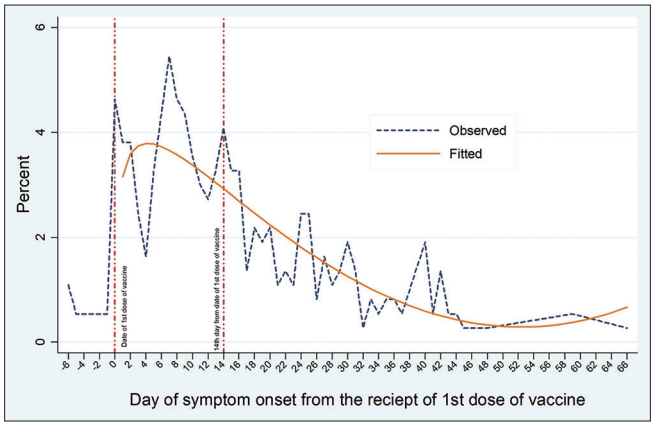

Figure 1: Temporal trends of symptom onset after 1st dose of the vaccine among those who received only one dose vaccine

14 days of receipt of vaccine yielded similar results. Subgroup analysis of patients among which the name of vaccine is available (160 individuals who received Covaxin and 158 who received Covishield), showed no significant differences in outcomes between the two varieties.

Discussion

This cohort study highlights various outcomes of SARS-COV-2 infection among those with breakthrough infection after vaccination compared to those who were unvaccinated or partially vaccinated. We found that the odds of developing hypoxia (or severe COVID-19), requiring ventilatory support, deteriorating to a critical condition during the hospital stay, and death due to COVID-19 were significantly lesser among those who were completely vaccinated compared to those who were not. Completing the vaccination schedule for COVID-19 significantly decreased the inflammatory response caused by the SARS-CoV-2 virus, thereby reducing the risk of developing serious complications during illness. Even receiving a single shot of the COVID-19 vaccine seemed to reduce the inflammatory response after 14 days of receiving the vaccine, making the individual less prone to severe COVID-19.

Of the 1748 patients in our study cohort, only 3% were completely vaccinated ($n = 53$). This can either be due to: (a) lower incidence of symptomatic SARS-CoV-2 infection among the completely vaccinated group, thus obviating the need for hospitalization, as evidenced by reports from India and other countries.[6,7,15,16] (b) or due to lower vaccination rates in the country before wave-2. The reported breakthrough infection rate among the vaccinated Indians was only 0.04% as of April 2021.[17] Only 4% of Indians were completely vaccinated by the end of June 2021.[18] The reasons for this could be manifold. Though the public hospitals were providing vaccines free of cost, the private players were also providing at a nominal rate of INR 250. It is not known if vaccine slot unavailability at public hospitals could have played a role in vaccine-seeking behavior, however, studies in past have reported that willingness to pay for the vaccine varies widely across the low- to middle-income countries.[19]

Approximately 18% of the breakthrough infections in our study cohort presented with moderate to severe COVID-19 and required oxygen support as compared to 62.4% in the unvaccinated group. Although this is relatively higher to 9.2% and 6.7% reported in studies by Sharma *et al*. and Tyagi *et al*. among breakthrough infections in Indian health care workers but is comparable to 18.6% reported by Sabnis *et al*.[8-10] However, studies from other countries such as Israel reported up to 66% of severe COVID-19 in breakthrough infections, but this study constituted mostly of older population with comorbidities.[20] In our study only two (4%) of the fully vaccinated individuals required mechanical ventilation compared to 16%–18% in unvaccinated or partially vaccinated

groups. This is comparable to the 4.7% need for mechanical ventilation among fully vaccinated individuals reported from the United States and Israel.[21,22]

We also noted that the requirement for use of steroids and antiviral agents in fully vaccinated was less compared to the unvaccinated or partially vaccinated group. This may be explained due to lesser incidence of hypoxia or requirement for oxygen in these individuals. Furthermore, lesser use of steroids may decrease the risk for hyperglycemia and mucormycosis in these individuals.[23] Less need for antiviral agents will also help in reducing the cost of therapy. Now with more studies confirming extra-pulmonary manifestations of SARS-CoV-2 infection, there is increasing evidence of evoking multi-organ dysfunction in addition to severe respiratory distress syndrome among the Covid-19 patients.[24,25] Our study shows that the proportion of those developing renal dysfunction during stay was significantly lesser in the fully vaccinated group (3·9%) compared to other study groups as shown in Table 3. Similarly, transaminitis occurred in a significantly lesser proportion of fully vaccinated individuals compared to others [Table 2]. This is also of importance in post-COVID-19 recovery as more and more studies on Post-COVID-19 syndrome report increased rates of multiorgan dysfunction even at 4 months after initial symptoms compared with the expected risk in the general population.[26]

Our results of fully vaccinated individuals having lower odds of requiring oxygen, receiving mechanical ventilation, deteriorating during the hospital stay, developing critical illness, and death as shown in Table 4 are in concordance with those reported from India and other countries.[11,12,21,27,28] Lesser need for oxygen supplementation and lower risk of death were also evident amongst those who received a single dose of vaccine, thus showing significant protection in this group as well. Another study from our center which compared outcomes between silent hypoxia and dyspneic hypoxia also reported that vaccination status is not significantly associated with outcomes among patients who developed hypoxia and the proportion of those with silent hypoxia is similar in vaccinated and unvaccinated groups.[29]

More individuals in the unvaccinated and partially vaccinated groups had a hyper-inflammatory response as evidenced by high d-Dimer, IL-6 and CRP levels as compared to fully vaccinated individuals. This may indicate that vaccination reduces the risk of developing hypoxia and cytokine storm, but once the patient develops hypoxia and ARDS, the odds of developing critical illness and death are similar to those of unvaccinated individuals. This is also consistent with studies which have shown that the pattern of inflammatory immune response determines the clinical course and outcome of COVID-19.[21,30]

Few limitations which could not be addressed due to the retrospective nature of this study are that 199 individuals in whom vaccination status was not available could not be included in the analysis among whom 21 (10·6%) died. Baseline ferritin and IL-6 marker profiles were available for very few in the final analysis cohort. Data regarding the baseline antibody titers before infection and the variant of SARS-CoV-2 are not available in these individuals.

Conclusions

In summary, our study shows that receiving both the doses of the vaccine protects the individual from developing severe COVID-19 and cytokine release syndrome as also reported by other vaccine efficacy trials and the world health organization. However, if vaccinated individuals develop severe COVID-19 and hypoxia due to other risk factors older age and comorbidities, they have a similar risk of death compared to that of unvaccinated individuals. COVID-19 vaccines available in India are effective in reducing the incidence of severe COVID-19, hypoxia, critical illness, and death. The reduced need for oxygen supplementation, mechanical ventilation, and the requirement of corticosteroids or other expensive medications such as anti-viral drugs could go a long way in redistributing scarce health care resources.

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Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: Comparison of the distribution of lab parameters and inflammatory markers across study groups

Lab parameters	Unvaccinated		Partially vaccinated		Fully vaccinated		overall and pairwise comparison			
	n	Median (p25-p75)	*n*	Median (p25-p75)	*n*	Median (p25-p75)	K-wallis - *P*	Unvaccinated versus partially vaccinated	Unvaccinated versus fully vaccinated	Partially versus fully vaccinated
Hemoglobin (mg/dL)	1221	13 (11.6-14.4)	188	13 (11.9-14.3)	42	13.8 (12.9-14.5)	0.018	1.000	0.007	0.02
Leucocyte count (cells/mm^3)	1217	7.7 (5.2-11.6)	188	7.4 (5.2-10.9)	42	5.9 (4.6-7.5)	0.027	1.000	0.011	0.033
Platelet count (10^3/µL)	1224	223 (162-310)	189	217 (159-279)	44	180.5 (144.5-233.5)	0.062	0.556	0.038	0.153
Neutrophil count (10^3/µL)	1183	6 (3.2-9.7)	183	5.6 (3.2-9.4)	40	3.9 (2.5-5.4)	0.002	0.882	0.001	0.005
Lymphocyte count (10^3/µL)	1183	0.9 (0.6-1.3)	183	0.9 (0.6-1.5)	40	1.3 (1.2-1.7)	<0.001	0.897	<0.001	<0.001
Total bilirubin (mg/dL)	1239	0.5 (0.4-0.7)	190	0.5 (0.4-0.7)	44	0.5 (0.4-0.6)	0.611	0.803	0.622	0.969
ALT (U/L)	1228	49 (29-86.5)	189	40 (24-66)	44	29 (22.5-48)	<0.001	0.005	<0.001	0.068
AST (U/L)	1228	49 (32-77.5)	189	40 (28-66)	44	32.5 (25.5-43.5)	<0.001	0.002	<0.001	0.018
Total protein (g/dL)	1229	6.4 (6-6.8)	188	6.5 (6-6.9)	44	6.8 (6.5-7.2)	<0.001	0.189	<0.001	<0.001
Alkaline phosphatase (U/L)	1228	80 (64-106)	189	76 (59-95)	44	80 (65.5-103)	0.013	0.005	1.000	0.301
Globulin (g/dL)	1218	2.6 (2.3-2.9)	186	2.6 (2.3-2.8)	43	2.7 (2.4-2.9)	0.299	0.551	0.344	0.192
Albumin (g/dL)	1228	3.8 (3.5-4.1)	189	3.9 (3.6-4.2)	44	4.3 (4-4.5)	<0.001	0.06	<0.001	<0.001
Albumin globulin ratio	1214	1.5 (1.3-1.7)	187	1.5 (1.3-1.7)	43	1.6 (1.4-1.8)	0.02	0.133	0.030	0.27
Urea (mg/dL)	1246	35.1 (24-53.5)	189	34.2 (23.5-55.6)	45	24 (19.3-30)	<0.001	1.000	<0.001	<0.001
Creatinine (mg/dL)	1245	0.7 (0.6-0.9)	190	0.8 (0.7-0.9)	45	0.8 (0.7-0.9)	0.036	0.029	0.321	1.000
Calcium (mg/dL)	1223	8.4 (8-8.7)	188	8.5 (8.1-8.9)	45	8.7 (8.4-9.1)	<0.001	0.007	<0.001	0.014
Sodium (mEq/L)	1236	138 (136-140)	190	138 (135-140)	45	139 (137-140)	0.62	1.000	0.538	0.498
Potassium (mEq/L)	1235	4.5 (4.1-5)	190	4.5 (4.1-4.9)	45	4.3 (3.9-4.5)	0.026	1.000	0.012	0.015
d-dimer (ng/mL)	1042	247 (149-532)	165	236 (140-485)	42	114.5 (75-187)	<0.001	0.501	<0.001	<0.001
Fibrinogen (mg/dL)	1057	416 (347-491)	163	416 (335-485)	39	364 (317-436)	0.014	0.828	0.006	0.028
Ferritin (ng/mL)	440	547 (193.8-1078.1)	65	357.1 (157.4-1106.6)	14	226.9 (107.4-511.6)	0.125	0.555	0.089	0.274
LDH	1058	400 (275-577)	158	311.5 (229-490)	40	223 (195-302.5)	<0.001	<0.001	<0.001	<0.001
CRP (mg/dL)	1166	3.8 (1.3-9.1)	181	4 (0.8-9.5)	44	1.1 (0.2-3.4)	<0.001	0.873	<0.001	0.001
IL-6 (pg/mL)	592	13.2 (5.4-38)	87	7·2 (2.6-22.9)	13	3.6 (2.1-17.7)	0.001	0.001	0.081	0.909

ALT: Alanine transaminase, AST: Aspartate transaminase, CRP: C-reactive protein, IL-6: Interleukin-6, LDH: Lactate dehydrogenase