ORIGINAL ARTICLE

Demographics and Clinical Characteristics of COVID-19-vaccinated Patients Admitted to ICU: A Multicenter Cohort Study from India (PostCoVac Study-COVID Group)

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Abstract

Background: Emergency authorization and approval were given for the coronavirus disease-19 (COVID-19) vaccines. The efficacy reported after phase III trials were 70.4% and 78% for Covishield and Covaxin, respectively.

In this study, we aim to analyze the risk factors, which were associated with mortality in critically ill COVID-19-vaccinated patients admitted into intensive care unit (ICU).

Materials and methods: This study was conducted from April 1, 2021 to December 31, 2021 across five centers in India. Patients who had received either one or two doses of any of the COVID vaccines and developed COVID-19 were included. The ICU mortality was a primary outcome.

Results: A total of 174 patients with COVID-19 illness were included in the study. The mean age was 57 years standard deviation (SD 15). Acute physiology, age and chronic health evaluation (APACHE II) score and the sequential organ failure assessment (SOFA) score were 14 (8–24.5) and 6 (4–8), respectively. Multiple variable logistic regression showed patients who have received a single dose [odds ratio (OR): 2.89, confidence interval (CI): 1.18, 7.08], neutrophil:lymphocyte (NL) ratio (OR: 1.07, CI: 1.02,1.11), and SOFA score (OR: 1.18, CI: 1.03,1.36) were associated with higher mortality.

Conclusion: The mortality in the vaccinated patients admitted to the ICU was 43.68% due to COVID illness. The mortality was lower in patients who had received two doses.

Keywords: BBV152, Breakthrough infection, ChAdOx1 nCOV19, Covaxin, COVID-19, COVID vaccination, Delta variant, ICU, Multicenter study.

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Highlights

- This study aimed to see the mortality in vaccinated patients who developed COVID-19 infection requiring ICU admission. The ICU mortality was 43.68%.
- Risk factors associated with mortality were single dose receivers, NL ratio, and SOFA score. The mortality observed in patients who received two doses was lower than single dose receivers.

Introduction

The global pandemic of COVID-19 has caused a significant impact on humanity and the economy. During the first wave, much has been talked about and researched about the novel virus, its epidemiology, clinical features, and possible treatment options. Within a year, scientists have developed a vaccine, as a possible tool to contain the pandemic.[1]

Vaccination offers protection against severe disease and reduces case fatality.[1–3] COVID vaccines were assessed to ensure quality, safety, and efficacy using the clinical trial data.[4] The vaccination drive was initiated by immunizing vulnerable people and frontline workers in January 2021 in India. Covishield (AstraZeneca/AZD1222) and the Bharat Biotech BBV152 Covaxin were approved based on the results of phase III trials. The reported efficacy from vaccination was 70.4 % and 78% for Covishield and Covaxin, respectively.[5,6] The efficacy of the vaccine may differ with the time interval between

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the doses. However, increasing the duration between the two doses may increase the risk of developing COVID-19 infection among partially vaccinated groups.[7]

The first study from Israel, evaluating the protective effects of the "Pfizer BioNTech mRNA COVID-19 BNT16b2" vaccine showed that two doses of the vaccine reduced symptomatic and asymptomatic infections, hospitalizations, severe disease, and death.[8] Similarly, a community-based study done in United Kingdom (UK) where three vaccines were licensed, Pfizer BioNTech mRNA COVID-19 BNT16b2', mRNA 1273 (Moderna), and ChAdOx1 nCoV-19 (Oxford-AstraZeneca), showed symptoms were rare in infected vaccinated individuals, predominantly observed in >60 years of age-group.[9] Due to the inherent nature of viruses to mutate, new variants with different presentations and epidemiological profiles were detected. Consequently, reduced neutralization of viruses by vaccine-induced antibodies was seen.[10,11]

To the best of our knowledge, there are enough community-based studies of post-vaccinated individuals, but the data about critically ill patients are lacking. We aimed to analyze the risk factors associated with mortality in vaccinated patients.

Materials and Methods

Study Population

A retrospective observational cohort study was conducted from April 1, 2021 to December 31, 2021, after institutional ethical committee approval (IEC 149/2021, Clinical Trials Registry India (CTRI) 2021/07/034587). A total of five centers were enrolled in the study. Patients >18 years of age who had received either first or second dose of any of the COVID vaccine and were admitted to ICU with COVID-19 and had positive reverse transcriptase-polymerase chain reaction (RT-PCR) or rapid antigen test were recruited in the study. We included patients who received the first or second dose of the vaccine irrespective of the number of days from the vaccination. Non-vaccinated patients were excluded from the study.

A sample size of 385 was sufficient to observe 50% mortality due to COVID-19 illness in these patients with 5% absolute precision. The observed mortality was 60% in COVID-19 patients from India who were intubated within 48 hours.[12] We used 50% as the expected mortality in our cohort anticipating a 10% reduction in mortality offered by vaccination based on the previous study.[13] Each enrolled center obtained IEC approval from the respective hospitals. The centers included were tertiary care centers and teaching hospitals. The ICU admission criteria were based on the treating team and respective hospital protocols.

Data Collection

Data collection was done in Excel Form. Details of the age, sex, comorbidities, type of vaccine received, number of doses, and time from vaccination to hospitalization were collected. Acute physiology, age and chronic health evaluation II score and SOFA score were calculated. Ventilator parameters, PaO_2/FiO_2 (PF ratio), type of oxygen device, mode of ventilation, tidal volume (TV), plateau pressure (P_{plat}), peak inspiratory pressure (P_{peak}), and positive end-expiratory pressure (PEEP) were collected. Driving pressure ($P_{plat\text{-}PEEP}$), static compliance (TV/$P_{plat\text{-}PEEP}$), and dynamic compliance (TV/$P_{peak\text{-}PEEP}$) were calculated. From day 1 to day 5 of ICU admission, all the available ventilator parameters were collected. We have chosen 5 days, anticipating a less severe and shorter duration of illness in the vaccinated patients.[8] The primary outcome was ICU mortality, defined as the condition of the patient at the time of ICU discharge. Secondary outcomes were ICU length of stay, duration of mechanical ventilation, and hospital mortality. The duration of mechanical ventilation was defined as the number of days patient was requiring invasive ventilator support from intubation till the ICU discharge or death as applicable. The Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines were followed while reporting the data.

Statistical analysis was done using STATA™ (Version 14, College station TX). The continuous data were reported as mean SD if the data were symmetric or as median (interquartile range, IQR) otherwise. Categorical data were reported as numbers (%). Univariate logistic regression was done to identify risk factors associated with ICU mortality. Many of the variables were found to be collinear. Hence, the careful selection of variables was made based on clinical importance. The unadjusted and adjusted odds ratio (95% CI) were reported. The trend of various parameters over 5 days was analyzed using the mixed linear model. All *p*-values less than 5% were considered statistically significant.

Results

A total of 901 patients were screened and 727 patients were excluded due to unvaccinated status or missing records. A total of 174 patients were included in the study (Supplementary material Figure S1) The mean age was 57 (SD = 15) and predominantly were men. Among the baseline parameters, age was significant with a difference of 5 years between non-survivors and survivors (60.30 vs 55.10, $p = 0.012$) (Table 1). The mortality was 39.68% and 54.17% in ≤65 and >65 years, respectively. The number of doses received was significant with single dose receivers had higher mortality (50.43% vs 29.82%). Details about the type of vaccination were available in 167 patients. Out of 166, 78.31% received Covishield and 21.69% received Covaxin. One patient received a single dose of Sputnik. For analysis, only two groups were considered. The mortality in Covaxin group was lower than that in Covishield group (25% vs 46.92%, $p = 0.018$). There was no effect of prior infection with COVID-19 on ICU mortality (Table 1).

Among the comorbidities, diabetes mellitus (DM), ischemic heart disease (IHD), chronic kidney disease (CKD), and hypertension were associated with higher mortality. The median APACHE II score on day 1 was 14 (8–24.5) and the median SOFA score was 6 (4–8).

Among day 1 parameters, the need for vasopressors and ABG pH were strongly associated with higher mortality. All the commonly used biomarkers were higher in non-survivors than survivors, except for procalcitonin and troponin I (Table 1).

Primary and Secondary Outcomes

The ICU mortality was 43.68%. The length of ICU stay and duration of mechanical ventilation were similar between the survivors and non-survivors. The hospital mortality was 46.55% (Table 1).

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Table 1: Sociodemographic and baseline characteristics

Parameter	*All (n = 174)*	*Survivors (n = 98)*	*Non-survivors (n = 76)*	*p value*
Age[¥]	57.54 (14.60)	55.10 (14.85)	60.30 (13.73)	*0.012
Age-groups (yrs)				
≤35	13 (7.47)	9 (9.18)	4 (5.26)	0.2
36–50	36 (20.69)	24 (24.49)	12 (15.79)	
51–65	77 (44.25)	43 (43.88)	34 (44.74)	
≥66	48 (27.59)	22 (22.45)	26 (34.21)	
Gender	M/F (121/53) (69.54/30.46)	M/F (65/33) (66.33/33.67)	M/F (56/20) (73.68/26.32)	0.3
Any vaccine: single dose/two doses	117/57 (67.24/32.76)	58/40 (59.18/40.82)	59/17 (77.63/22.37)	*0.010
Type of vaccine Covishield vs Covaxin	130/36 (78.31/21.69)	69/27 (71.88/28.13)	61/9 (87.14/12.86)	*0.018
Time from vaccination to hospitalization	33.5 (16.50–66.5)	41 (20–90)	29 (15–59)	0.052
Time between two doses	40 (31–59)	43 (32–65)	31 (29–52)	0.039
APACHE II score	14 (8–24.5)	10 (7–16)	21 (14–31)	*<0.01
SOFA score	6 (4–8)	4 (3–7)	8 (5–12)	*<0.01
DM	70 (40.23)	31 (31.63)	39 (51.32)	*0.009
Hypertension	62 (35.63)	24 (24.49)	38 (50)	*<0.001
ACE inhibitors	9 (17.65)	5 (20.83)	4 (14.81)	0.57
ARB	17 (33.33)	7 (30.43)	10 (35.71)	0.69
CLD	5 (2.87)	2 (2.08)	3 (3.95)	0.455
CKD	10 (5.75)	0 (0)	10 (13.16)	*<0.001
CVA	3 (1.72)	0 (0)	3 (3.95)	0.047
IHD	18 (10.34)	4 (4.08)	14 (18.42)	*0.002
COPD	4 (2.30)	3 (3.06)	1 (1.32)	0.45
Bronchial asthma	5 (2.87)	2 (2.04)	3 (3.95)	0.45
ILD	2 (1.15)	1 (1.02)	1 (1.32)	0.85
TB	2 (1.15)	1 (1.02)	1 (1.32)	0.85
Immunosuppressants	2 (1.15)	2 (2.04)	0 (0)	0.21
Malignancy	4 (2.30)	2 (2.04)	2 (2.63)	0.79
Similar complaints in close contacts	45 (25.86)	34 (34.69)	11 (14.47)	*0.003
History of contact with COVID-positive patient	18 (10.34)	11 (11.22)	7 (9.21)	0.66
History of contact with COVID-suspect patient	34 (19.54)	20 (20.41)	14 (18.42)	0.74
Prior infection with COVID	21 (12.14)	13 (13.40)	8 (10.53)	0.56
Prior COVID infection required ICU care	9 (5.77)	7 (7.95)	2 (2.94)	0.18
History of fever	104 (59.77)	46 (46.94)	58 (76.32)	*<0.001
Cough	82 (47.13)	39 (39.80)	43 (56.58)	*0.028
Shortness of breath	95 (54.60)	44 (44.90)	51 (67.11)	*0.004
Sore throat	14 (8.05)	10 (10.20)	4 (5.26)	0.235
Running nose	14 (8.05)	10 (10.20)	4 (5.26)	0.235
Use of NIV prior to ICU	27 (23.68)	6 (10.34)	21 (37.50)	*0.001
Use of HFNC prior to ICU	24 (22.02)	9 (16.07)	15 (28.30)	0.124
ABG PH Day 1	7.38 (0.11)	7.40 (0.07)	7.34 (0.13)	*<0.001
Pt requiring vasopressors on Day 1	26 (14.94)	9 (9.18)	17 (22.37)	*0.016
Need for RRT	8 (6.5)	2 (3.39)	6 (9.38)	0.17

(Contd...)

Table 1: *(Contd...)*

Parameter	*All (n = 174)*	*Survivors (n = 98)*	*Non-survivors (n = 76)*	*p value*
Need for blood transfusion	15 (10.27)	8 (10.67)	7 (9.86)	0.87
NL ratio[§]	8.97 (5.40–15.17)	7.78 (4.59–11.25)	12.36 (7.36–23.50)	*<0.001
Ferritin[§]	783.10 (446.40–1409.90)	587 (350–1160)	1015.60 (562–2190.10)	*0.005
Procalcitonin[§]	0.33 (0.15–1.00)	0.15 (0.05–0.31)	0.16 (0.01–0.34)	0.55
D-dimer[§]	963 (545–1834)	855 (537–1388.50)	1050 (600–2547)	*0.027
LDH[§]	607 (385–829)	505 (300–674)	726 (505–889)	*0.009
CRP[§]	31 (7.62–78)	45 (11.73–110)	15.10 (6.34–40)	*0.006
Troponin I[§]	0.03 (0.01–0.12)	0.02 (0.01–0.48)	0.03 (0.01–0.07)	0.546
From hospital admission to ICU admission[§]	0 (0–3)	0 (0–3)	0 (0–2)	0.40
Outcomes				
Secondary outcomes				
Hospital mortality		93 (53.45)	81 (46.55)	
ICU length of stay[§]	8 (4–14)	8 (4–13)	8.5 (3–14.5)	0.60
Days on mechanical ventilation[§]	7 (4–9)	7 (4–9)	7 (4–8)	0.77

ACE, angiotensin-converting enzyme; ABG, arterial blood gas; ARB, angiotensin receptor blocker; CLD, chronic liver disease; CKD, chronic kidney disease; CVA, cerebrovascular accident; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; HFNC, high-flow nasal cannula; ILD, interstitial lung disease; LDH^{-}, lactate dehydrogenase; NIV, non-invasive ventilation; NL ratio, neutrophil: lymphocyte ratio; RRT, renal replacement therapy; TB, tuberculosis; Values are *n* (%), *p* value from Chi-square test of association; [¥]Mean (SD), independent sample *t*-test was used for comparison; [§]Median (IQR), *p* value from Mann–Whitney *U* test. Units of measurement D-dimer, ferritin, procalcitonin and troponin I (ng/mL), CRP (mg/dL), and LDH (U/L). **p*-value <0.05

The use of noninvasive ventilation (NIV) prior to ICU admission was one of the risk factors associated with mortality. The requirement of invasive ventilator support and lower PF ratio was significantly associated with mortality. Among ventilator parameters, only dynamic compliance was significant with higher values in survivors than non-survivors (24.71 vs 19 mL/cm H_2O, $p = 0.026$). The PCO_2 was higher in non-survivors than in survivors (47.34 vs 39.13, $p \leq 0.001$) (Table 2).

There was no significant increasing or decreasing trend for parameters including PF ratio, driving pressure, static and dynamic compliance over 5 days and this was not significantly different between survivors and non-survivors by mixed linear model analysis, although the PF ratio continued to remain higher in survivors (Fig. 1). The mean values of static and dynamic compliance were higher and driving pressure was lower for the first 4 days in survivors.

Out of 174 patients, 46 were intubated on the day 1 of ICU. Proning as a rescue strategy for improving oxygenation was used in 21.74 % (10/46) of intubated patients and awake proning was used in 31.25% (40/128) patients. Proning was used in similar proportions among survivors and non-survivors (Table 2).

Details about treatment received were collected. Steroid was used in 70.69% of patients (Table 2). This study was not aimed to evaluate the effect of various therapies.

The risk factors associated with ICU mortality were identified by univariate logistic regression. (Supplementary material Table S1) We also studied the hospital-wise difference in mortality and included it as one of the variable in the analysis. The final multiple variable logistic regression showed single dose receivers (OR: 2.89, CI: 1.18,7.08), NL ratio (OR: 1.07, CI: 1.02,1.11), and SOFA score (OR: 1.18, CI: 1.03,1.36) were significant covariates (Table 3). The discrimination of the model was good as shown by the receiver operating characteristic curve ($p = 0.82$). (Supplementary material Figure S2)

Mortality

Additional analysis with respect to number of doses received was performed (Table 4). The higher odds for the ICU mortality was observed OR: 2.28 (CI: 1.17–4.43) for single dose receivers.

Discussion

This is one of the largest studies, which evaluated risk factors and ICU mortality in patients who developed breakthrough COVID-19 infections post-vaccination. The ICU mortality was 43.68% (36.18–51.38%) Patients who had received two doses had lower mortality 29.82% (18–43%) as compared to single dose receivers 50.43% (41–59%).

Various community-based studies are published on the effectiveness of vaccination, breakthrough infections, and cohort studies on healthcare workers developing a COVID-19 infection.[8,9]

The study done in Israel showed vaccination reduced symptomatic as well as asymptomatic infections, and an increase in the vaccination coverage resulted in lesser infections in a population.[8]

A case–control study, using a community-based app done in the UK showed rates of both symptomatic and asymptomatic infections and the need for hospitalization were lower in vaccinated people.[9]

The test negative case–control study from UK evaluating the effectiveness of BNT16b2 and ChAdOx1 nCoV-19 vaccine against B.1.167.2 (delta) variant included symptomatic COVID-19 patients vs symptomatic test negative patients as control. The vaccination status of these patients was compared. Genome sequencing was done to find out a particular variant. The findings were two doses as compared to a single dose against delta variant infection were effective.[14] This is similar to our study. There were certain differences as we included all RT-PCR positive patients and it was a retrospective study.

Table 2: Oxygen therapy and ventilator parameters

Day 1 parameters	*All*	*Survived (n = 98)*	*Nonsurvived (n = 76)*	*p-value*
Type of oxygen therapy				
HFNC	16 (13.11)	9 (11.11)	7 (17.07)	0.069
NIV	37 (30.33)	20 (24.69)	17 (41.46)	
NRBM	35 (28.69)	23 (28.40)	12 (29.27)	
Other devices	27 (22.13)	23 (28.40)	4 (9.76)	
Room air	7 (5.74)	6 (7.41)	1 (2.44)	
PF ratio	113.33 (82.27–175)	145.63 (92.14–213.33)	100 (75.56–147)	0.002
Worst FiO_2 on Day 1[¥] of ICU	79.58 (18.56)	75.22 (19.24)	83.78 (17.02)	0.019
Day 1 Invasive ventilation	46 (26.44)	13 (13.27)	33 (43.42)	<0.001
TV[¥] Min	365 (47.46)	376 (66.88)	362 (39.94)	0.366
TV [¥] Max	438 (133.61)	449 (95.09)	434 (144.53)	0.732
TV[¥] min mL/kg	5.60 (0.97)	5.92 (1.03)	5.46 (0.93)	0.175
TV[¥] max mL/kg	6.63 (1.66)	6.81 (1.25)	6.55 (1.82)	0.657
PEEPmax[¥]	9.67 (2.94)	8.63 (2.83)	10.11 (2.90)	0.065
Plateau pressure[¥]	29.03 (8.87)	25.6 (6.69)	29.85 (9.26)	0.345
Peak inspiratory[¥] pressure	28.80 (12.04)	22.35 (8.83)	31.29 (12.26)	0.008
Driving pressure[¥]	16.5 (12–22)	15 (12–18)	17 (12–23)	0.453
Static compliance[§]	24.71 (17.27–31.67)	26.39 (20.56–33.11)	24.71 (17.27–31.67)	0.528
Dynamic compliance[§]	19.27 (15.20–42)	2 4.71 (20–79.80)	19.00 (12.26–33.33)	0.026
PO_2 (min)[¥]	76.98 (22.37)	77.69 (19.28)	76.20 (25.47)	0.694
PO_2 (max)[§]	94 (75–124)	98.65 (76.90–128)	90 (68.20–113)	0.280
PCO_2 (min)[¥]	35.92 (9.17)	33.62 (5.47)	38.45 (11.51)	0.001
PCO_2 (max)[¥]	43.18 (14.40)	39.13 (8.28)	47.57 (17.99)	<0.001
Fluid balance[§]	50 (–50 to –640)	0 (0–605)	297.5 (–250 to –900)	0.665
Prone positioning	50 (29.59)	29 (29.59)	21 (27.63)	0.77
Treatment received				
Steroid	123 (70.69)	59 (60.20)	64 (84.21)	<0.001
Remdesivir	58 (33.33)	32 (32.65)	26 (34.21)	0.829
Tocilizumab	5 (2.87)	2 (2.04)	3 (3.95)	0.455
Baricitinib	19 (10.92)	16 (16.33)	3 (3.95)	0.009
Tofacitinib	10 (5.75)	6 (6.12)	4 (5.26)	0.809
Favipiravir	3 (1.72)	2 (2.04)	1 (1.32)	0.716
Bevacizumab	2 (1.15)	0 (0)	2 (2.63)	0.106

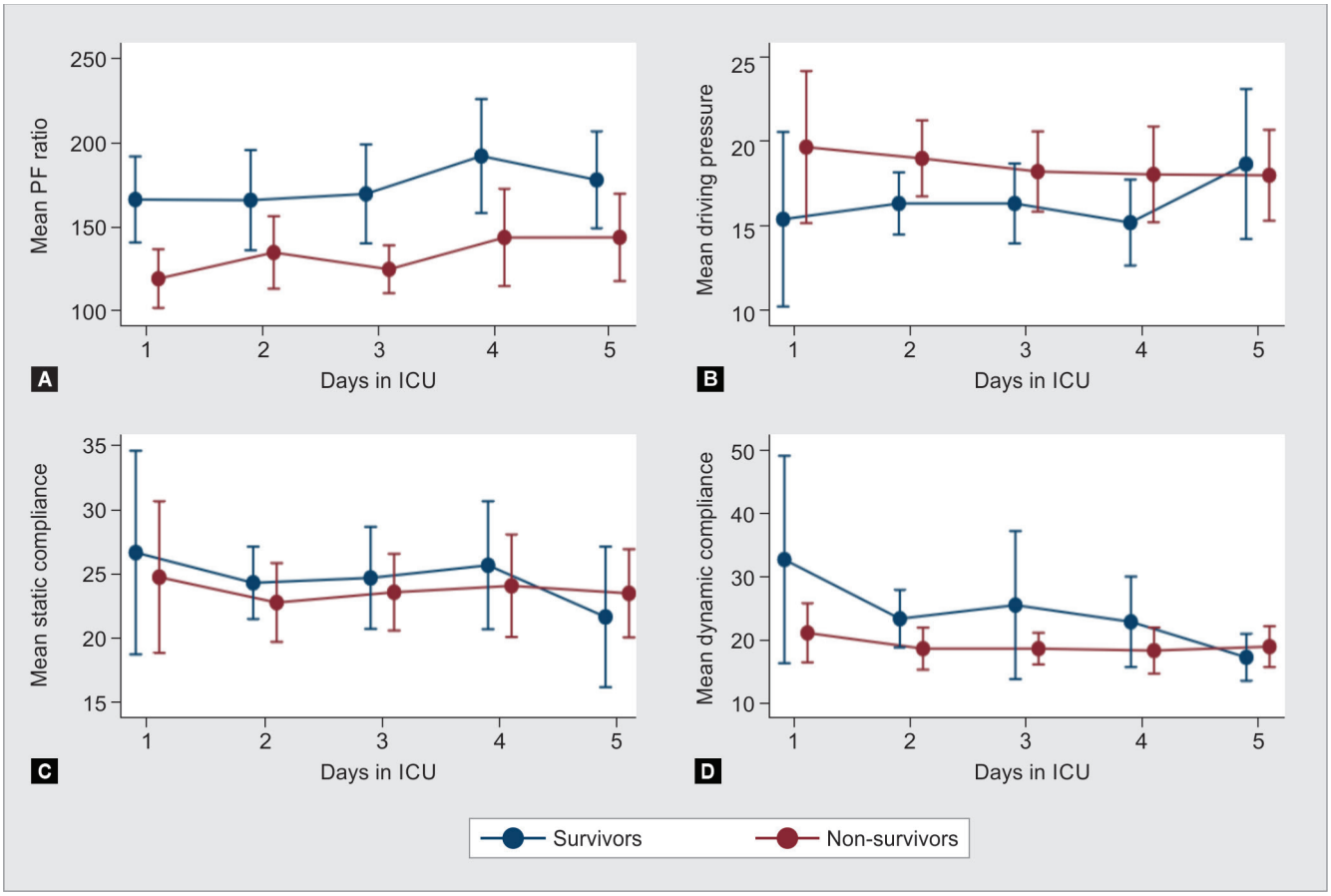
NRBM, non-rebreathing mask; PF, ratio-PaO_2/FiO_2 ratio; TV, tidal volume; Values are *n* (%), *p*-value from Chi-square test of association; [¥]Mean (SD), independent sample *t*-test was used for comparison; [§]Median (IQR); Mann–Whitney *U* test was for comparison. Units of measurements: PO_2, PCO_2 (mmHg)

The study from South India evaluating mortality in vaccinated patients admitted to the hospital showed lower mortality in a fully vaccinated group as compared to a partially vaccinated group as defined in this study. The severely ill patients were 6.4% and 1.2% in partially vaccinated and fully vaccinated groups.[15] The mortality observed in this study was lower compared to our study. Reasons for higher mortality in our study were patients with severe COVID-19 requiring intensive care admission were included and out of which 26.44% were requiring invasive ventilator support on the day 1 of ICU admission.

The initial single-center pilot study evaluating the rate and severity of infection among vaccinated healthcare workers showed the healthcare workers infected with COVID-19 were less, but also the COVID-19 infection was less severe and no adverse outcome was seen.[16] The multicenter study on healthcare workers from the same investigators also showed lesser symptomatic infections and less severe illness.[17]

The reasons for less severe illness observed in studies involving healthcare workers could be early reporting of symptoms and initiation of treatment. Also awareness about the COVID-19 infection and use of COVID appropriate behavior like the use of social distancing, masking, and handwashing practices.[18] As the majority of healthcare workers had received two doses thereby lower incidence of infection was observed in this cohort. Our study included the general population, this could have resulted in delayed presentation and higher mortality. Among 174 patients, we had only 1 healthcare worker (0.57%).

There are various strengths to our study. This is the only multicenter study evaluating risk factors associated with the mortality in critically ill vaccinated (received single or two doses



Figs 1A to D: Trend of parameters over 5 days. Blue circles indicate trend of parameters in survivors and red circles indicate trend of parameters in non-survivors. (A) PF ratio; (B) Driving pressure; (C) Static compliance; (D) Dynamic compliance

Table 3: Multiple variable logistic regression of risk factors associated with the ICU mortality

Parameters	*N*	*Adjusted odds ratio (95% CI)*	*p-value*
Age	174	1.019 (0.989,1.049)	0.209
Number of doses	174	2.89 (1.18,7.08)	0.020
History of IHD	174	2.50 (0.64,9.75)	0.186
Day 1 invasive ventilation	174	2.17 (0.71,6.63)	0.173
NL ratio	171	1.07 (1.02,1.11)	0.003
History of DM	174	1.54 (0.67–3.56)	0.306
SOFA score	168	1.18 (1.03–1.36)	0.014
Hospital-wise	174	1.14 (0.79–1.65)	0.457

of vaccines, Covishield/Covaxin) patients admitted to ICU. We included the general population in our study and not limited to a particular cohort; hence, the findings of our study will have wider applicability.

The limitations of this study are not including the control group of unvaccinated patients as it was a cohort study with ICU mortality as a primary outcome, survivors as an internal control. The inclusion of patients 14 days after the second dose would have helped in knowing the actual effectiveness of vaccination. In our study, only 28 out of 174 (16.09%) patients were admitted within 14 days of vaccination. The patients who had received a single dose were included based on the protection offered by a single dose.[14] The monitoring of antibody titers post-vaccination (anti spike protein antibodies) and its relation with the severity of illness would have helped in identifying patients who had immune escape phenomenon leading to a lack of antibody response post-vaccination, resulting in a severe illness.[19] Due to the lesser number of patients in the Covaxin group, we did not analyze the effect of the type of vaccine on ICU mortality. This observation needs to be studied in a larger cohort. Due to a decrease in COVID-19 cases by December 2021 and change in the virus strain, from Delta variant to Omicron, causing lesser severity of infection, and reduced intensive care admissions across all the centers, we did not enroll patients after December and target sample size of 385 could not be achieved. Although the proposed sample size for estimating the mortality rate with 5% precision could not be achieved, the sample size of 117 and 57 was sufficient to observe a 20% difference in mortality with 80% power in patients who received single dose vs two doses of COVID-19 vaccination.

Considering the retrospective study design, identification of a particular virus strain by genome sequencing was not possible. The studied population largely reflects the infection with the Delta strain based on the timing of the study (April 2021 to December 2021) and the prevalent COVID strain during the study duration.

Table 4: Patient characteristics based on the number of doses received

Parameter	*All (n = 174)*	*Single dose (n = 117)*	*Double dose (n = 57)*	*Odd's ratio*	*95% CI*
Age[¥]	57.58 (14.67)	55.60 (14.88)	61.78 (13.38)	0.96	0.94–0.99
Gender	M/F (121/53) (69.54/30.46)	M/F (83/34) (70.94/29.06)	M/F (38/19) (66.37/33.33)	0.81	0.41–1.61
Time from vaccination to hospitalization	33.5 (16.50–66.5)	24 (15–48.5)	61.5 (27–102.50)	0.98	0.97–0.99
ICU mortality	78 (44.83)	60 (50.43)	18 (29.82)	2.28	1.17–4.43
DM	70 (40.23)	43 (36.75)	27 (47.37)	0.64	0.33–1.22
Hypertension	62 (35.63)	42 (35.90)	20 (35.09)	1.036	0.53–2.00
ACE inhibitors	9 (17.65)	7 (20)	2 (12.50)	1.75	0.32–9.55
ARB	17 (33.33)	10 (28.57)	7 (43.75)	0.51	0.15–1.75
CLD	5 (2.87)	4 (3.42)	1 (1.75)	1.98	0.21–18.15
CKD	10 (5.75)	7 (5.98)	3 (5.26)	1.14	0.28–4.60
CVA	3 (1.72)	2 (1.71)	1 (1.75)	0.97	0.08–10.97
IHD	18 (10.34)	13 (11.11)	5 (8.77)	1.3	0.43–3.84
COPD	4 (2.31)	3 (2.56)	1 (1.75)	1.47	0.14–14.48
Bronchial asthma	5 (2.87)	4 (3.42)	1 (1.75)	1.98	0.21–18.15
ILD	2 (1.15)	1 (0.85)	1 (1.75)	0.48	0.02–7.86
TB	2 (1.15)	1 (0.85)	1 (1.75)	0.48	0.02–7.86
Malignancy	4 (2.31)	3 (2.56)	1 (1.75)	1.47	0.14–14.48

Values are *n* (%), *p*-value from Chi-square test of association; [¥]Mean (SD), Independent sample *t*-test was used for comparison

This study showed that ICU mortality was 43.68% (36.18–51.38%) in vaccinated patients who developed severe COVID and were admitted to the ICU. For patients who had received two doses of vaccine there was 20 % reduction in ICU mortality. Hence, vaccination is one of the effective strategies to offer protection from the disease and contain the pandemic and has significant implications on public health.

Supplementary Materials

The supplementary materials is available online on the website of www.ijccm.org.

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