Original Article

A study on clinicodemographic profile, severity, and outcome of Covid-19 in hospitalized vaccinated individuals at tertiary care centre

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ABSTRACT

Objective: To evaluate the demographic profile, clinical severity, and outcome of Covid-19 infection in hospitalised vaccinated individuals. **Methods:** An observational, cross-sectional study was conducted among Covid-19 infected hospitalised patients. Clinicodemographic profile, severity, and outcome of Covid-19 infection among the vaccinated group (VG) were recorded. These patients were also compared with unvaccinated group (UVG) with Covid-19 infection admitted during the study period. Cox proportional hazards models was used to estimate hazard ratios for mortality risk in both groups. **Results:** Out of 580 participants, 48.2% were vaccinated with either one (71%) or two doses (28.9%). In both, VG and UVG, majority 55.8% belonged to 51–75 years. Males were predominant with 62.9% in both VG and UVGs. Day of illness at admission from symptom onset (DOI), progression of disease, ICU stay, oxygen requirement, mortality was significantly higher in UVG than in VG ($p < 0.05$). Steroid duration ($p < 0.001$) and anti-coagulation time ($p < 0.001$) were significantly higher in UVG than in VG. D dimer levels were significantly higher in UVG than in VG ($p < 0.05$). Increased age, ($p < 0.0004$), severity of disease, ($p < 0.0052$), increased oxygen requirement ($p < 0.001$), elevated C-reactive protein levels (Moderate: $P < 0.0013$; Severe $P < 0.0082$), and elevated IL-6 levels ($p < 0.001$) were the significant determinants of Covid-19-related mortality in both VG and UVGs. **Conclusion:** Vaccinated individuals have shown milder severity, had reduced hospital stay and better outcomes as compared to unvaccinated individuals suggesting a potential vaccine efficacy against Covid-19.

KEY WORDS: Covid-19 disease severity, Covid-19 outcome, and mortality, Covid-19 vaccine status

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Submitted: 12-Jan-2022 **Revised:** 25-Jul-2022 **Accepted:** 13-Nov-2022 **Published:** 28-Apr-2023

INTRODUCTION

The global impact of the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus on human health is indefinable.[1] As of October 4, 2021, globally, 234,609,003 people were affected and SARS-CoV-2 caused 4,797,368 deaths. India has evidenced 33,834,702 confirmed SARS CoV-2 infection cases and 448,997

Access this article online

Quick Response Code:

Website: https://journals.lww.com/lungindia

DOI: 10.4103/lungindia.lungindia_28_22

How to cite this article: Gali JH, Shah C, Keerthi BY, Thomas V. A study on clinicodemographic profile, severity, and outcome of Covid-19 in hospitalized vaccinated individuals at tertiary care centre. Lung India 2023;40:215-21.

deaths.[1] Hence, with the ongoing pandemic fatigue for appropriate Covid-19 behaviour, testing, isolation, and lockdown, mass vaccination is the most influential public health drive to end this deadly pandemic.[2]

Since 2020, countries worldwide worked diligently to develop an effective vaccine to reduce the risk of infection and severity of disease in infected individuals by boosting natural immune defences.[2] Vaccination roll-out across the world have shown that the introduced Covid-19 vaccines have been effective against serious Covid-19 infection across all ages in preventing symptomatic and asymptomatic SARS-CoV-2 infections and Covid-19-related hospitalizations, severe disease, and death.[3,4] Vaccination against Covid-19 infection was launched in India in January 2021, currently, vaccines approved for emergency use are Covishield (Oxford-AstraZeneca vaccine), Covaxin (Bharat Biotech) and Sputnik V (Moscow's Gamaleya Institute) with Covishield and Covaxin being widely used.[5] Ministry of Health and Family Welfare, Government of India (MOHFW, GOI) has undertaken a massive vaccination drive in India, to develop herd immunity. The efficacy rate of vaccines varies, as on 3rd March 2021, COVAXIN and COVISHIELD had a reported efficacy rate of approximately about 81% and 70%, respectively.[6]Unexpectedly, breakthrough Covid-19 infections have been reported to occur among partially vaccinated individuals and fully vaccinated individuals.[7]

As there is limited data and very few studies have been published in India about the demographic profile, clinical presentation, and outcomes of Covid-19 infection in vaccinated individuals, we aimed to evaluate the clinicodemographic profile, severity and outcome of disease in post vaccinated individuals who received COVISHIELD or COVAXIN and also compare them with unvaccinated individuals.

SUBJECTS AND METHODS

A prospective, hospital-based, observational, cross-sectional study was conducted for 4 months from April 2021 to July 2021 at a state-run exclusive Covid-19 tertiary centre where lower- and middle-income populations seek health care facilities. The study was approved by the Institutional Scientific Research Committee [SRC number - TIMS/2020-21/14 on 11/08/2021] and verbal informed consent was obtained from all the participants. All participants hospitalized with confirmed Covid-19 infection either by rapid antigen testing (RAT) or reverse-transcriptase-polymerase-chain-reaction (RT-PCR) were included. Patients either admitted or referred from other centres with end stage diseases in debilitating conditions for Covid-19 care were excluded from the study. Based on the vaccination status subjects were divided into unvaccinated group (UVG) and vaccinated group (VG). Patients who were infected 2 weeks after single/double dose of either vaccine were categorized as vaccinated group (VG; $n = 280$).[8,9] Patients without any prior vaccination were categorized as unvaccinated group (UVG; $n = 300$). Unvaccinated group participants were randomly selected at the interval of every 5th case, fitting the study criteria.

Breakthrough infections were defined as having positive laboratory testing for SARS-CoV-2 and/or symptom onset >14 days after the second dose of either vaccine.[8,9]

The patients' demographic details, important clinical status, relevant laboratory parameters, treatment data and outcome (recovery, death and persisting symptoms) were documented. All patients were graded for clinical severity at admission as mild, moderate, or severe according to the Indian Council for Medical Research (ICMR) classifications.[10] Early and late presentation were categorized based on admission cut-off of 7 days since many of the severe manifestations tend to occur as many as 8 to 14 days after symptom onset and portend worsened outcomes.[11] One month after hospitalisation, to note any persisting symptoms, a follow up was conducted by a trained physician without any leading questions to avoid bias.

Statistical analysis

The data were analyzed using Stata/IC 16.1. (StataCorp LP, College Station, TX, USA) or Graph pad prism, version 9. Confidence intervals were set at 95% and values of $P < 0.05$ were interpreted as statistically significant. Categorical variables were presented in the form of a frequency table. Continuous variables were presented as Mean ± Std. Deviation (SD)/Median (Min, Max) form. A Chi-square test was applied to find the association of attributes. Two sample *t* test/Mann–Whitney *U* test was used to compare mean/distributions of parameters over the groups. We used Cox proportional hazards models to estimate hazard ratios (HRs) for mortality risk in both VG and UVG Covid-19 patients.

RESULTS

Out of the 689 admitted patients, 109 were excluded and 580 were studied [Supplementary Material Figure 1], of which 48.2% ($n = 280$) were vaccinated. Of the 280 vaccinated subjects, 71% ($n = 199$) took one dose, 28.9% ($n = 81$) took two doses of vaccination and majority 79.29% ($n = 222$) had taken COVISHIELD and 20.71% ($n = 58$) took COVAXIN. In both groups, majority 55.8% ($n = 324$) belonged to 51–75 years. Males 62.9% ($n = 365$) were predominantly affected in both groups. Day of illness at admission from symptom onset (DOI), hospital stay, severity at admission, progression of the disease, ICU stay, oxygen requirement, mortality rate was significantly higher in UVG than VG [$p < 0.05$; Table 1 and 2].

The duration of hospital stay (≥3 weeks) was more in UVG than VG. [Supplementary Material Table 2].

Table 1: Comparison of demographic, clinical profiles, and inflammatory markers between vaccinated and unvaccinated Covid-19 patients

Variables	Sub-category	VG	UVG	Total	*P*
Age (years)	18-25	6 (2.14%)	5 (1.67%)	11 (1.9%)	0.6657[C]
	26-50	111 (39.64%)	111 (37%)	222 (38.28%)	
	50-75	150 (53.57%)	174 (58%)	324 (55.86%)	
	>75	13 (4.64%)	10 (3.33%)	23 (3.97%)	
	Mean±SD	53.49±14.72	54.13±13.49	53.82±14.09	0.5876[WT]
	Median (Min, Max)	55 (21, 91)	55 (19, 94)	55 (19, 94)	
Gender	Female	100 (35.71%)	115 (38.33%)	215 (37.07%)	0.514[C]
	Male	180 (64.29%)	185 (61.67%)	365 (62.93%)	
Day of illness at	<7	200 (71.43%)	183 (61%)	383 (66.03%)	0.008[C]*
Admission from	≥7	80 (28.57%)	117 (39%)	197 (33.97%)	
symptom onset	Mean±SD	5.58±3.06	6.17±3.7	5.88±3.42	0.0358[MW]*
	Median (Min, Max)	5 (1, 23)	5 (1, 30)	5 (1, 30)	
Hospital Stay	1 week	145 (51.79%)	104 (34.67%)	249 (42.93%)	<0.001[C]*
	2 weeks	108 (38.57%)	130 (43.33%)	238 (41.03%)	
	3 weeks	21 (7.5%)	50 (16.67%)	71 (12.24%)	
	More than 3 weeks	6 (2.14%)	16 (5.33%)	22 (3.79%)	
	Mean±SD	8.59±4.94	10.47±6.04	9.56±5.61	<0.001[C]*
	Median (Min, Max)	7 (1, 48)	10 (1, 33)	8 (1, 48)	
Comorbidity	Multiple	97 (34.64%)	125 (41.67%)	222 (38.28%)	0.0705[C]
	Single	90 (32.14%)	100 (33.33%)	190 (32.76%)	
	No Comorbidity	93 (33.21%)	75 (25%)	168 (28.97%)	
Severity Stage at	Mild	185 (66.07%)	83 (27.67%)	268 (46.21%)	<0.001[C]*
admission	Moderate	44 (15.71%)	87 (29%)	131 (22.59%)	
	Severe	51 (18.21%)	130 (43.33%)	181 (31.21%)	
Progression	No progression	261 (93.21%)	238 (79.33%)	499 (86.03%)	<0.001[C]*
	Moderate	9 (3.21%)	16 (5.33%)	25 (4.31%)	
	Severe	10 (3.57%)	46 (15.33%)	56 (9.66%)	
Oxygen duration (days)	Mean±SD	3.14±5.51	7.32±6.16	5.31±6.21	<0.001[MW]*
	Median (Min, Max)	0 (0, 48)	7 (0, 27)	4 (0, 48)	
ICU stay (days)	Mean±SD	1.16±2.9	3.39±3.94	2.31±3.65	<0.001[MW]*
	Median (Min, Max)	0 (0, 20)	2.5 (0, 21)	0 (0, 21)	
HB	Mean±SD	12.47±1.86	12.53±1.68	12.5±1.77	0.6551[MW]
	Median (Min, Max)	12.5 (6.7, 19)	12.5 (6.7, 17.5)	12.5 (6.7, 19)	
Total leucocyte	Mean±SD	9.22±4.48	9±4.25	9.1±4.36	0.6619[MW]
count (TLC)	Median (Min, Max)	8.01 (3.04, 28.68)	7.95 (2.78, 29.95)	7.98 (2.78, 29.95)	
Neutrophil	Mean±SD	7.63±4.35	7.55±4.03	7.59±4.19	0.9568[MW]
	Median (Min, Max)	6.41 (0.83, 27.38)	6.78 (2.04, 28.06)	6.48 (0.83, 28.06)	
Lymphocyte	Mean±SD	1.22±1	1±0.74	1.11±0.88	0.008[MW]*
	Median (Min, Max)	0.99 (0.02, 5.9)	0.8 (0.13, 5.9)	0.86 (0.02, 5.9)	
Neutrophil/Lymphocyte	Mean±SD	12.73±24.21	11.92±11.78	12.31±18.82	0.0386[MW]*
ratio	Median (Min, Max)	6.83 (0, 346)	7.9 (0.94, 76.46)	7.36 (0, 346)	
Platelet count	Mean±SD	230.62±92.97	219.33±89.43	224.78±91.25	0.0381[MW]*
	Median (Min, Max)	225.5 (0.54, 755)	206.5 (0.58, 755)	216 (0.54, 755)	
CRP	Mild	117 (41.79%)	109 (36.33%)	226 (38.97%)	<0.001[C]*
	Moderate	53 (18.93%)	156 (52%)	209 (36.03%)	
	Normal	99 (35.36%)	22 (7.33%)	121 (20.86%)	
	Severe	11 (3.93%)	13 (4.33%)	24 (4.14%)	
D dimer	Mean±SD	0.73±1.16	0.86±0.89	0.8±1.03	<0.001[MW]*
	Median (Min, Max)	0.41 (0.01, 9.51)	0.68 (0.05, 9.51)	0.58 (0.01, 9.51)	
IL 6	Mean±SD	36.63±45.3	34.77±24.21	35.67±35.95	0.0053[MW]*
	Median (Min, Max)	22.5 (0.37, 308)	32.1 (0.78, 128)	25.9 (0.37, 308)	
Steroid duration (days)	Mean±SD	3.54±5.79	7.91±6.73	5.8±6.65	<0.001[MW]*
	Median (Min, Max)	0 (0, 36)	7 (0, 31)	4 (0, 36)	
Anti-Coagulation	Mean±SD	3.56±5.85	7.93±6.72	5.82±6.68	<0.001[MW]*
duration (days)	Median (Min, Max)	0 (0, 38)	7 (0, 31)	4 (0, 38)	
Outcome	Death**	23 (8.21%)	44 (14.67%)	67 (11.55%)	0.0151[C]*
	Recovered	257 (91.79%)	256 (85.33%)	513 (88.45%)	

C - Chi-square test, MW - Mann Whitney U test, * indicates statistical significance. **Death among those who took one dose was 10% (*n*=20) and among those who took two doses was 3.7% (*n*=3)

16.8% had breakthrough infections of which 80.8% had mild course of disease and none of them required >3 weeks of hospital stay.

There is significant association between number of doses taken and severity of disease in VG [$p < 0.001$, Supplementary Material Table 3]. Among the deceased,

14.6% deaths were noted among UVG, 10% among those who took one dose and only 3.7% among individuals who took two doses. Even though there was no statistical significance for comorbidities [$p = 0.22$, Supplementary Material Table 4], the number of deaths among individuals with multiple comorbidities was lesser in VG compared to UVG.

Among UVG, weakness (66.3%,) was the most common persistent symptom whereas among the VG, 13.5% reported weakness after 1 month.

Estimation of hazard ratio for each patient characteristic from a multivariable Cox model

From multivariate Cox proportional hazard model, increased age, the severity of disease, increased oxygen duration, elevation in C-reactive protein levels, Interleukin-6 levels are significant determinants for Covid-19-related death [Table 3 and Figure 2] in both VG and UVGs. With 1-year increase in age, hazard increases by 1.04 (95% CI: 1.02 – 1.06). Hazard increases by 0.8 (95% CI: 0.76–0.85) with 1 day increase in oxygen duration. Risk of death is 3.94 (95% CI: 1–15.5) times higher for subjects with moderate disease and 6.17 (95% CI: 1.72–22.07) times higher for subjects with severe disease compared to the subjects with mild disease. Subjects with moderate CRP level have 6.71 (95% CI: 2.1–21.46) times and subjects with severe CRP level have 5.69 (95% CI: 1.57–20.65) higher risk of death compared to the subjects with mild CRP. Hazard increases by factor 1.02 (95% CI: 1.01–1.02) with unit increase in IL-6 [Table 3 and Figure 2].

DISCUSSION

In our study, 280 individuals were infected with Covid-19 post vaccination. Of these, 71% (199) were infected after taking first dose of vaccine and 28.9% (81) were infected post two doses, showing that hospital admissions after two doses of vaccination were significantly lower disclosing that complete vaccination prevent disease progression. Israel was the first country that reported 22 laboratory-Covid-19 cases among health care workers postimmunization with Pfizer-BioNTech Covid-19 vaccine.[12]

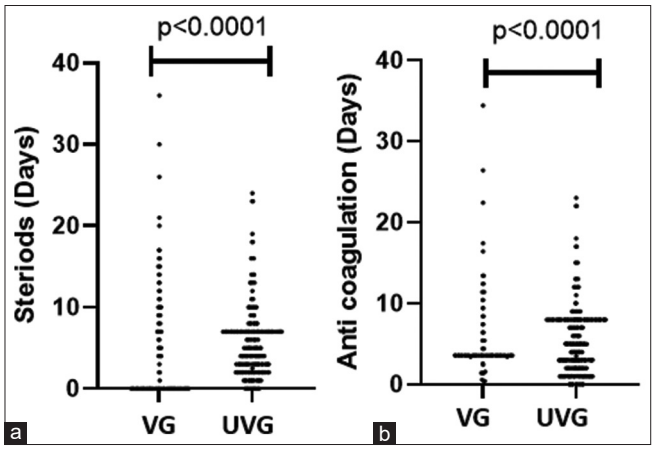

Figure 1: Forest Plot on comparison of steroid usage and anti-coagulation time between vaccinated and unvaccinated Covid-19 patients. VG – Vaccinated group (partially vaccinated and fully vaccinated individuals), UVG – unvaccinated group. Steroid duration; $P < 0.001$; a) and anti-coagulation time ($P < 0.001$; b) were significantly higher in UVG than in VG

In our study, among both VG and UVG, majority (55.8%) belonged to 51–75 years age group followed by 26–50 years age group (38.2%), as Covid 19 is associated with advanced illness among older population. Males (62.9%) were predominantly affected in both VG and UVGs. In a similar study by Muthukrishnan *et al*.,[13] 1,168 patients were included in the study and had a male preponderance with a mean age of 54.6 (± 17.51) years.

In our study, 61% ($n = 183$) of UVG, 67.33% ($n = 134$) of those infected after first dose, 81.48% ($n = 66$) of those infected after second dose presented within 7 days of illness, which reflects that awareness regarding infection and seeking medical help was proportionately more among VG. Late admissions (>7 days) can be attributed to common beliefs that symptoms are due to seasonal viral infection, weather changes or post vaccination than of Covid-19 infection. [Supplementary Material Table 5].

Among the VG, patients infected after first dose of vaccine were more in number (199 vs. 81) as compared to second probably because till April 30, 2021, Covid vaccines in India were only available in Government centres and gap between first and second dose of COVISHIELD was extended from 28 days to 6–8 weeks in March 2021, which was further extended to 12–16 weeks in May 2021. Though the gap between first and second dose of COVAXIN was 28 days, its supply was limited and was not easily available. Due to lonf with long intervals between both doses, patients were infected while being partially immunized. Other reasons for more infections after first dose such as general presumption of complete protection after first dose, possibly led to public disregard of Covid appropriate behaviour. Therefore, this reaffirms the need for educating the masses for completing their vaccination course, identifying Covid-19 symptoms, and seeking timely medical help.

In our study, among the VG, the mean duration from last dose of vaccine to symptom onset (>14 days) in individuals who took single dose was 26.11 ± 23.75 SD and in those who took two doses of vaccination was 26.06 ± 23.75 SD which emphasizes that individuals may not be completely immune to the ever-evolving SARS-CoV 2 virus, however, vaccination imparts protection and aids in reducing the severity, course of illness and provides better outcomes. However, we cannot extrapolate this to general population since this data includes only symptomatic hospitalized patients.

The duration of hospital stay (≥3 weeks) was more in UVG than VG and none of the individuals who took two doses

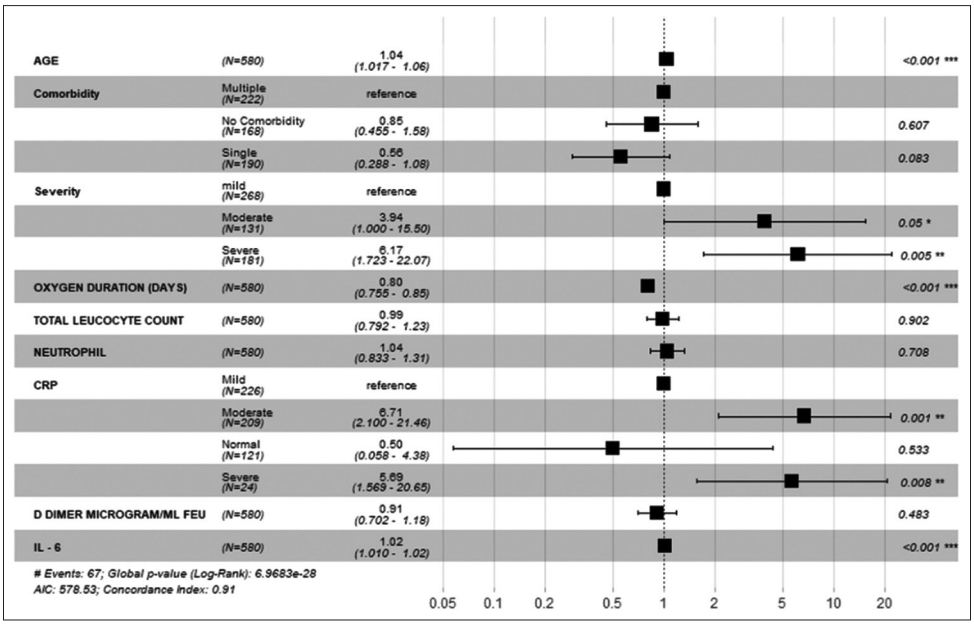

Figure 2: Estimated hazard ratios for each patient characteristic from a multivariable Cox model. Note: Cox proportional hazard model is done for each variable, and the significant variables are included in the multivariate Cox proportional hazard model. Hazard ratios are shown on a log scale. Error bars represent the limits of the 95% confidence interval for the hazard ratio

required >3 weeks of hospital stay. We also observed, the hospital stay was significantly longer in patients who were admitted late to the hospital in both VG and UVGs ($p = < 0.01$; Table 1).

The unvaccinated group showed significantly elevated neutrophil/lymphocyte ratio, C-reactive protein levels, and D-dimer levels compared to the vaccinated group ($p < 0.05$). In a similar study by Sagiraju *et al*.,[14] more individuals in the unvaccinated and partially vaccinated groups had a hyper-inflammatory response as evidenced by high d-Dimer and CRP levels as compared to fully vaccinated individuals. We also observed that 18.6% (108) of both VG and UVGs, had moderate to severe anaemia**.** Similarly, another study suggested that age and presence of anaemia were positively associated with Covid-19 infection post vaccination.[8]

In our study, 16.8% individuals had breakthrough infections and majority (80.8%) had mild course of illness with a maximum of 2 weeks hospital stay. In a similar study by Tyagi *et al*.,[15] breakthrough COVID19 infections (≥14 days after the second dose) occurred in 13.3% and all had mild COVID19 disease. Previous studies demonstrated that irrespective of the high incidence of SARS-CoV-2 infections due to variant strains, fully vaccinated individuals remained substantially less likely to seek emergency care or become hospitalized.[8,16,17] In this study, among VG, 66% 15.7% and 18.21% whereas 27.6%, 29% and 43.3% of the UVG subjects, got admitted in mild, moderate and severe stage respectively [Supplementary Material Table 1]. We also observed that fewer partially or completely vaccinated patients with Covid-19 infection progressed to a severe stage after hospital admission [Table 1].

Vaccinated participants were likely to be more asymptomatic, especially those who are >60 years and are more prone for adverse outcomes.[13,18] However, in our study, both VG and UVG patients with advanced age (>60 years) were symptomatic at presentation since our hospital is a Covid-19 tertiary care centre. In our study, it was noted that vaccination provided protection by reducing disease severity and progression of disease, duration of hospital and ICU stay, steroid use, anti-coagulation usage, oxygen requirement, and reducing persisting symptoms [Supplementary Material Table 2] Longer steroid and anti-coagulation usage, elevated D-dimer and IL–6 levels contribute to chronic inflammation, decreased immunity, and increased disease severity in Covid-19 patients.[19,20] Similarly, in an another study by Kumar *et al*.[5] severity of disease (3.2% vs. 7.2%; $P = 0.0039$) and requirement of ventilatory support (2.8% vs. 5.9%; $P = 0.0154$) were significantly lower in the VG even though these individuals had significantly higher age and additional risk factors [Figure 1].

In our study, mortality was 45% lower in VG when compared to UVG. A similar study by Kumar *et al*.,[5] reported that the mortality rate was about 50% lower (1.51%) in the completely vaccinated group and deceased vaccinated individuals had advanced age and higher comorbidity burden when compared to unvaccinated individuals and partially vaccinated group. In few other studies by Muthukrishnan *et al*.,[13] Sagiraju *et al*.[14] and Hippisley-Cox *et al*.,[21] there was 12.5%, 5.7%, and 3.98% mortality observed among fully vaccinated individuals respectively.

Butt *et al*.[7] and Juthani *et al*.,[22] postulated that older persons have a higher burden of comorbidities, and an ineffective immune response could be mounted against vaccines among those with comorbidities that may predispose them to poorer clinical outcomes. Similarly, in our study, the mean age among those who succumbed to disease was higher among VG as compared UVG (62.48 ± 12.16 vs. 60 ± 12.73). 14.6% (44) deaths were noted in UVG while only 3.7% (3) after two doses of vaccination. All these 3 deaths were seen in elderly (mean age 75.33 years) with multiple comorbidities who got admitted in advanced stage of disease, with immediate causes of death being sudden cardiac arrest after acute MI, atrial fibrillation and ARDS with severe COVID-19 respectively. Similarly, increased age, severity of disease, increased oxygen duration, elevated C-reactive protein, D dimer and Interleukin-6 levels are the significant independent risk factors associated with Covid-19-related death in both VG and UVGs [Tables 2 and 3]. In a similar study by Butt *et al*.[7] increasing age (HR vs. <40 years age: >40–60 years, HR 2.32; >60–70 years, HR 4.34; >70 years, HR 5.43); symptoms at baseline (HR 2.42, 95% CI 1.44–4.07); and being unvaccinated (HR 2.84, 95%CI 1.80–4.47) were the significant factors for poorer clinical outcome in patients with Covid-19 infection. However, in our study, although statistically insignificant, we observed a clinical association between comorbidities and adverse outcomes, indicating that vaccination is beneficial irrespective of the number of comorbidities. Similarly, study by Butt *et al*.,[7] found the presence of comorbidity status did not associate with severity of the disease or death in the vaccinated or unvaccinated patients [Supplementary Material Table 3 and Table 3].

We observed that a subgroup of hospitalized vaccinated individuals infected after first dose (21, 10.5%) and after second dose (10, 12.3%) probably were asymptomatic, later became symptomatic within 5 days of vaccination. Progression of disease was noted only among those infected after first dose. Thus, we speculate that the vaccine over stimulated the already primed immune system of these asymptomatic patients by SARS-CoV-2 and making them symptomatic. However, further larger studies are required to substantiate this hypothesis.

Strengths of study

Ours being a tertiary care centre, catering not only for treatment of moderate to severe cases, but also has facility for isolation of mild Covid 19 cases. As this study was done in a single centre, all patients were given same standard of care and treatment, all patients were under direct supervision, treatment and follow up by researchers, thereby minimizing errors in treatment and data collection.

Limitations

The study was conducted at a state run Covid-19 centre, leading to more Covishield recipients as in our state of Telangana, for initial few months of 2021, Covaxin was available only in private centres and in limited quantity. Other vaccines such as Sputnik V recipients were not included in the study due to limited availability of doses.

As our study is a hospital-based study, catering mostly to symptomatic Covid-19 infected patients among both vaccinated and unvaccinated group, we cannot extrapolate our results or comment explicitly on the efficacy of the vaccines against SARS-CoV-2 infection amongst general population.

Table 2: Stepwise logistic regression model

Variables	Estimate	Odds Ratio (95% CI)	*P*
Intercept	−0.2142	0.8072 (0.7271, 0.8961)	0.0001*
Age (years)	0.0029	1.0029 (1.0012, 1.0045)	0.0006*
Severity of disease (Ref: Mild)			
Moderate	0.0080	1.0081 (0.9339, 1.0881)	0.8372
Severe	0.1049	1.1106 (1.0172, 1.2125)	0.0196*
Neutrophil	0.0075	1.0076 (1.002, 1.0132)	0.0084*
CRP (Ref: Mild)			
Moderate	0.1372	1.147 (1.0761, 1.2226)	<0.001*
Normal	−0.0111	0.989 (0.9286, 1.0534)	0.7310
Severe	0.1948	1.215 (1.0692, 1.3807)	0.0029*
Oxygen duration	−0.0118	0.9883 (0.9826, 0.9941)	<0.001*
IL-6	0.0017	1.0017 (1.001, 1.0025)	<0.001*
ICU stay (Days)	0.0130	1.0131 (1.0035, 1.0228)	0.0076*

Abbreviation: *indicates statistical significance

Table 3: Hazard ratios and 95% confidence intervals for Covid-19-related death in both vaccinated and unvaccinated patients

Variables	Coefficient	Hazard Ratio (95% CI)	*P*
Age (years)	0.04	1.04 (1.02-1.06)	0.0004*
Comorbidity (Ref: Multiple)			
No Comorbidity	−0.16	0.85 (0.45-1.58)	0.6066
Single Comorbidity	−0.58	0.56 (0.29-1.08)	0.0831
The severity of disease (Ref: Mild)			
Moderate	1.37	3.94 (1-15.5)	0.0499*
Severe	1.82	6.17 (1.72-22.07)	0.0052*
Oxygen duration (days)	−0.22	0.8 (0.76-0.85)	<0.001*
Total leucocyte count	−0.01	0.99 (0.79-1.23)	0.9017
Neutrophil	0.04	1.04 (0.83-1.31)	0.7081
C-reactive protein (Ref: Mild)			
Normal	−0.69	0.5 (0.06-4.38)	0.5332
Moderate	1.90	6.71 (2.1-21.46)	0.0013*
Severe	1.74	5.69 (1.57-20.65)	0.0082*
D-dimer	−0.09	0.91 (0.7-1.18)	0.4829
Interleukin-6	0.02	1.02 (1.01-1.02)	<0.001*

Abbreviation: *Indicates statistical significance (p value < 0.001)

CONCLUSION

Vaccinated Covid-19 infected patients have shown milder severity, had reduced hospital stay and better outcomes as compared to unvaccinated individuals suggesting a potential vaccine efficacy against Covid-19 infection.

Advanced age, chronic disease burden, and delay in seeking medical help were the important contributing

factors for progression of disease in both vaccinated and unvaccinated individuals.

In conclusion, along with measures to curb the infection such as masking, social distancing, and hand hygiene, we stress upon the need for complete vaccination to enable optimal protection from Covid-19 infection. We further recommend that early medical advice should be sought if anyone develops symptoms despite their vaccination status. However, as our results do not reflect the general population demographics, larger population inclusive studies and longitudinal multicentric studies are warranted to validate the current findings.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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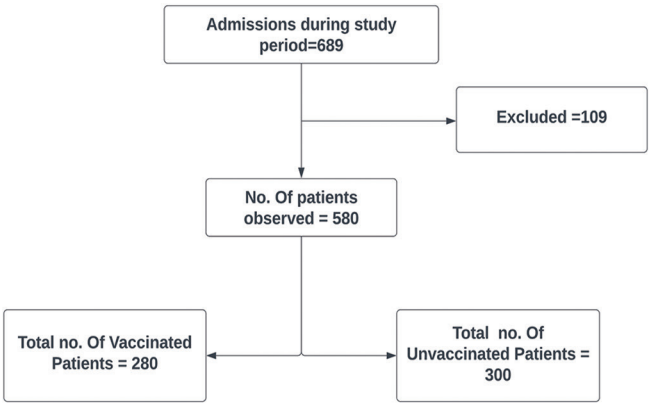

Supplementary Material Figure 1: Flow chart depicting study recruitment

Supplementary Material Table 1: Additional data on comparison of clinicodemographic profile and outcome of unvaccinated, vaccinated with first dose and second dose individuals

	Unvaccinated (*n*=300)	Vaccinated with 1 dose (*n*=199)	Vaccinated with 2 doses (*n*=81)	*P*
Age				
≤50	116 (38.66%)	91 (45.72%)	26 (32.09%)	0.08
>50	184 (61.33%)	108 (54.27%)	55 (67.9%)	
Mean±SD	54.1±13.5	53.53±14.75	53.07±14.96	0.9996
	54.2±13.39	53.53±14.76	53.46±14.8	
Day of illness at admission from symptom onset				
<7 days	183 (61%)	134 (67.33%)	66 (81.48%)	0.002*
≥7 days	117 (39%)	65 (32.6%)	15 (18.51%)	
Mean±SD	6.16±3.70	5.57±3.06	5.46±2.90	0.999
	6.19±3.71	5.58±3.06	5.63±3.13	
Severity at admission				
Mild	83 (27.6%)	121 (60.8%)	64 (79%)	0.001*
Moderate	87 (29%)	35 (17.58%)	9 (11.1%)	
Severe	130 (43.33%)	43 (21.6%)	8 (9.87%)	
Hospital Stay				
1 week	104 (34.66%)	105 (52.76%))	40 (49.38%)	0.001*
2 weeks	130 (43.33%)	72 (36.18%)	36 (44.44%)	
3 weeks	50 (16.66%)	16 (8.04%)	5 (6.17%)	
>3 weeks	16 (5.33%)	6 (3.01%)	0	
Outcome				
Death	44 (14.6%)	20 (10%)	3 (3.7%)	0.02*
Recovered	256 (85.33%)	170 (85.42%))	78 (96.29%)	

C - Chi-square test, * indicates statistical significance

Supplementary Material Table 2: Comparison of different variables with outcome among both groups

Variables	Sub-category	Death	Recovered	*P*
Vaccinated Group (VG)				
Oxygen duration (days)	Mean±SD	7.78±10.79	2.73±4.58	<0.001[MW]*
	Median (Min, Max)	5 (0, 48)	0 (0, 23)	
ICU stay (days)	Mean±SD	5.09±5.34	0.81±2.27	<0.001[MW]*
	Median (Min, Max)	4 (0, 20)	0 (0, 16)	
Hospital stay	1 week	14 (60.87%)	131 (50.97%)	0.0895[MC]
	2 weeks	6 (26.09%)	102 (39.69%)	
	3 weeks	1 (4.35%)	20 (7.78%)	
	More than 3 weeks	2 (8.7%)	4 (1.56%)	
Unvaccinated Group (UVG)				
Oxygen duration (days)	Mean±SD	7.14±5.65	7.36±6.25	0.8924[MW]
	Median (Min, Max)	7 (0, 21)	7 (0, 27)	
ICU stay (days)	Mean±SD	5.11±4.69	3.09±3.72	<0.001[MW]*
	Median (Min, Max)	4 (0, 21)	2 (0, 20)	
Hospital stay	1 week	21 (47.73%)	83 (32.42%)	0.056[MC]
	2 weeks	14 (31.82%)	116 (45.31%)	
	3 weeks	9 (20.45%)	41 (16.02%)	
	More than 3 weeks	0	16 (6.25%)	

Abbreviation: MW - Mann-Whitney *U* test, MC - Chi square test with Monte Carlo simulation, * indicates statistical significance

Supplementary Material Table 3: Association of comorbidity and number of doses of vaccination with severity of disease

Variables	Subcategory	Mild	Moderate	Severe	Total	*P*
Comorbidity	No comorbidity	83 (49.4%)	28 (16.6%)	57 (33.9%)	168	0.29[C]
	Multiple	98 (44.1%)	55 (24.7%)	69 (31%)	222	
	Single	87 (45.7%)	48 (25.2%)	55 (28.9%)	190	
Dose of vaccination	0	83 (27.6%)	87 (29%)	130 (43.33%)	300	<0.001C*
	1	121 (60.8%)	35 (17.58%)	43 (21.6%)	199	
	2	64 (79%)	9 (11.1%)	8 (9.87%)	81	

Abbreviation: C - Chi square test, *indicates statistical significance

Supplementary Material Table 4: Comparison of age and comorbidity with outcome

Variables	Sub-category	Death	Recovered	*P*
Case				
Age (years)	Mean±SD	62.48±12.16	52.68±14.68	0.0021[t]*
	Median (Min, Max)	61 (45, 91)	55 (21, 85)	
Comorbidity	Multiple	11 (47.83%)	86 (33.46%)	0.2263[C]
	Single	4 (17.39%)	86 (33.46%)	
	No Comorbidity	8 (34.78%)	85 (33.07%)	
Control				
Age (years)	Mean±SD	60±12.73	53.12±13.38	0.0017[t]*
	Median (Min, Max)	59 (34, 87)	53 (19, 94)	
Comorbidity	Multiple	20 (45.45%)	105 (41.02%)	0.8523[C]
	Single	14 (31.82%)	86 (33.59%)	
	No Comorbidity	10 (22.73%)	65 (25.39%)	

Abbreviation: *t* - Two sample *t* test, C - Chi square test, * indicates statistical significance

Supplementary Material Table 5: Comparison of Day of illness at Admission from symptom onset with outcome

Day of illness at Admission from symptom onset	Death	Recovered	*P*
Vaccinated Group (VG)			
<7	10 (43.48%)	190 (73.93%)	0.002[C]*
≥7	13 (56.52%)	67 (26.07%)	
Mean±SD	7.61±4.88	5.39±2.78	0.0053[MW]*
Median (Min, Max)	7 (2, 23)	5 (1, 19)	
Unvaccinated Group (UVG)			
<7	21 (47.73%)	162 (63.28%)	0.046[C]*
≥7	23 (52.27%)	94 (36.72%)	
Mean±SD	7.09±3.44	6.01±3.73	0.0195[MW]*
Median (Min, Max)	7 (2, 15)	5 (1, 30)	

Abbreviation: C - Chi square test, MW - Mann-Whitney *U* test, *indicates statistical significance