



To Determine the Clinical Efficacy of COVID Vaccine in Post Vaccinated Individuals with Severe Pneumonia in Preventing ICU Mortality in a COVID Designated Tertiary Care Centre: A Retrospective Study

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ABSTRACT

Background: The "Severe Acute Respiratory Syndrome Coronavirus 2 disease has caused globally a challenging and threatening pandemic (COVID-19), with massive health and economic losses [1]. In India national vaccination campaigns kick started officially on January 16, 2021, and the vaccines were prioritized for frontline workers and susceptible groups. Individual vaccination can prevent or minimise a number of outcomes, including lab confirmed infection, symptomatic illness, infectivity rate, or a combination of these [2-3]. India had initially approved two vaccines under the trade name Covishield and Covaxin against COVID.

Aim: Demonstrate the efficacy of a single / two -dose schedule of COVID vaccine in the prevention of ICU mortality.

Methods: In this retrospective study, we included all COVID 19 confirmed patients who were admitted in covid designated ICU from March 15 to July 31 2021. Demographic, clinical, laboratory and radiological data were collected from all patients received in ICU. Primary outcome was to assess the mortality outcome in vaccinated COVID patients. Secondary outcome measured were to find an association between severity of the pneumonia and comorbidities, PaO₂/Fio₂ ratio, Neutrophil lymphocyte ratio, D dimer and CT severity score.

Results: 319 patients were enrolled in the study. 252 patients were not vaccinated. 59 had received the first dose and 8 patients had received both the doses. The mortality among vaccinated patients were less compared to nonvaccinated and significant (p value 0.030). Mortality among single and double dose vaccinated patients couldn't be made out because only 8 patients had received both the doses. Among the demographic profile, difference in age between vaccinated and unvaccinated was statistically significant. (64.39 ±11.916/ 54.18±14.124 p<.001. Among comorbidities hypertension, diabetes, obesity was associated with significant mortality. Admission saturation and mean PaO₂/FiO₂ ratio were high among vaccinated and significant. Neutrophil lymphocyte ratio, D dimer CT severity score were high among non vaccinated compared to vaccinated. There is no difference in mode of oxygen delivery in both vaccinated and non vaccinated patient. Days of ICU stay was less among vaccinated.

Conclusion: Effectiveness of vaccine against SARS-CoV-2 infection after the first dose of immunisation is convincingly evident. However second dose of immunization should be continued to attain total protection.

The authors declare no conflicts of interest.

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The global COVID pandemic has ravaged thousands of lives and disrupted the lives of billions of people. Drug controller of India had approved use of two vaccines Covishield and Covaxin, which helped in reducing the mortality and to get the pandemic under control. Covishield, manufactured and marketed by Serum Institute of India is a viral vector vaccine in which spike proteins are injected and it mounts a tolerable immune response to live virus. Covaxin manufactured by Bharat Biotech, uses an inactive dead virus that drafts an immune response [4-5].

Government of India started vaccine administration for COVID in January 2021. As of November 2021, around 1.21 billion doses had been administered, including first and second doses of the currently-approved vaccines. At least 80% of the eligible population received one dose, and number of fully vaccinated has exceeded those who have partially vaccinated.

The first phase of the vaccine coverage involved health and frontline workers. The next phase of the vaccine rollout covered all residents over the age of 60, and residents between the ages of 45 and 60 with comorbidities. Vaccine for general public started on March 1st 2021 for age 45 to 60 years with no comorbidities.

Methods

In this single centre retrospective study, all patients who had been received in COVID ICU from March 15 to July 31st 2021 were included in the study. After approval of institute ethical committee, we included all confirmed cases from March 15 to July 31. Cases were confirmed by RT-PCR and were analysed for demographic, clinical, laboratory and radiological data. Patient case sheets were accessed from medical record section. Patients with SpO₂<94% on room air, a respiratory rate >30 breaths/min, PaO₂/FiO₂<300 mm Hg, or lung infiltrates >50%, rapid clinical deterioration were considered as severe COVID [6]. Patients with acute respiratory distress syndrome, cardiac dysfunction, thrombotic disease were considered as critically ill.

The aim of this study was to estimate the frequency of COVID-19 death in people who received at least one or two doses of vaccine. Sampling method used was non probability sampling. The inclusion criteria were all patients of age greater than 18, fifteen days post vaccination, with RT PCR positive requiring ICU admission. Exclusion criteria were ICU patients without COVID-19, COVID patients under 18 years of age,

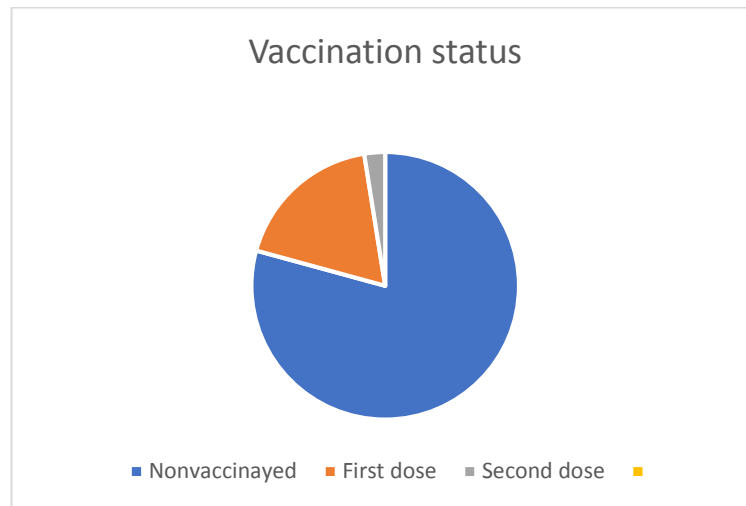
patients with mild to moderate symptoms, with no respiratory distress, no signs of pneumonia on lung radiography or tomography. All vaccinated patients treated in ICU received covishield vaccine. March 15th was taken as cut off because the vaccine drive for common public was started on March 1st. Vaccine efficiency is judged by its ability to protect against severe disease, and decrease the transmissibility in a community, as critical-care admissions poses the greatest burden on health-care systems.

Statistical analysis

All statistical analysis was performed with the SPSS version 20.0 (Statistical Package for the Social Sciences). The data were initially analysed for normality with Kolmogorov-Smirnov test. Baseline characteristics with continuous variables were presented as median with interquartile range (IQR) and categorical variables as number with percentage. Comparisons between continuous variables were tested by the Student t test and Mann-Whitney test based on variable distribution, and chi square test for categorical variables. A two-sided P value less than .05 was considered statistically significant.

Results

342 patients were received in ICU, finally 319 patients were enrolled for the study. Out of 23 dropouts few case sheets were incomplete and few patients died within 12 hours of admission. 252 patients were not vaccinated, 59 had received the first dose and 8 patients had received both the doses. (Figure 1) The mortality among vaccinated patients were less compared to nonvaccinated and significant p value 0.030. Mortality among single and double couldn't be made out because only 8 patients had received both the doses. There was a definitive gender variability with male preponderance. (Males 217/Females 102 p value=0.055). There was a statistically significant difference in age between vaccinated and unvaccinated (64.39 ±11.916/ 54.18±14.124 (p<.001). There was a significant association of mortality with comorbidities such as hypertension, diabetes, and obesity. The admission saturation and PF ratio was high in vaccinated population. Neutrophil lymphocyte ratio, D dimer CT severity score were high among nonvaccinated compared to vaccinated. There is no difference in mode of oxygen delivery in both vaccinated and nonvaccinated patient. The length of hospital stay was less in vaccinated patients.

Figure 1- Vaccination status of patient in ICU

Discussion

COVID-19 is a life-threatening disease that can have long-term sequelae. As the virus has a tendency to mutate vaccine efficacy is complex in the case of SARS-CoV-2, where the fundamental understanding of the pathogen is still questionable. There might not be a single vaccine which will cover up all variants SARS-CoV-2. We need a methodical framework for assessing vaccine efficacy endpoints to draw constructive conclusion and

comparison. All patients in our study were vaccinated with Covishield. There was a male preponderance and this was coinciding with the study of study of Docherty [7-9]. There was a statistically significant difference in age between vaccinated and unvaccinated. [64.39 ±11.916/ 54.18±14.124 (p<.001)] This finding is because phase 2 vaccination was started only for population above 60 and people with comorbidities. The mortality among vaccinated patients were less compared to non vaccinated and significant [10-13] (Table 1).

Table 1- Association between vaccination status and mortality

		vaccine status		Total
		No dose	Either 1 or 2 dose	
Outcome	Death	216	50	266
	Discharge	36	17	53
Total		252	67	319

Chi-square test; p value=0.030

There was a significant association of mortality with comorbidities such as diabetes (p=0.006), hypertension, (p=0.001) obesity (p=0.05). This finding was consistent with Chen et al,9 that people with hypertension and cardiovascular disease formed a major chunk among non survivors than survivors. These findings suggested that COVID-19 has a preponderance towards elderly with chronic comorbidities due to fragile immune functions. Admission saturation and PaO₂/FiO₂ ratio was high among vaccinated and significant (spo₂ 83.79±12.355/PF ratio 118.30±60.079 among vaccinated and 79.56±15.97 /101.43±50.13 in nonvaccinated (p=.035/.04). Neutrophil lymphocyte ratio among nonvaccinated group (median: 47.56; interquartile range [IQR]: 24.71-69.70) was higher than that of vaccinated group (median: 8.12; IQR: 3.44-8.12; P<.001). These results suggest that high NLR at the time of admission is associated with high mortality among patients with COVID-19. The virus damages lymphocytes, and hampers immune function during the course of the disease [14-15].

D dimer was greater than 2000 among nonvaccinated compared to vaccinated and (p=.051). Serum D-dimer were higher in patients with severe COVID compared to those with non-severe forms. In our study D-dimer levels values were 3-fold higher in those with severe disease (median: 2.12 mg/L; IQR: 0.77–5.27 mg/L) than in those with-out (median: 0.61 mg/L; IQR: 0.25–1.28 mg/l p<0.003). Cytokine storm induced by SARS-CoV triggers coagulation cascade, resulting in thrombotic complications. Therefore, patients with increased D-dimer should be started on antithrombotic therapies [16-18].

34% among non-vaccinated had thrombocytopenia and 18 % among vaccinated had thrombocytopenia (p value=.042). None of the patient platelet count decreased to a level that caused bleeding. Panyang Xu had concised the causes of thrombocytopenia in patients with COVID-19 and proposed a mechanisms by which COVID-19 causes thrombocytopenia [19].

CT severity score was high among nonvaccinated compared to vaccinated (Table 2). The CT score of the

vaccinated patients was significantly lower compared to unvaccinated patients (median 3.5 v. 9.5 respectively $p < .01$). Severity of the CT score is lowered by vaccination and hence improves survival outcome of the patient. Non vaccinated patients with comorbidities have higher CT scores in comparison to the vaccinated patients with comorbidity. Available data suggest that the vaccinated patients have better outcomes in terms of survival than

nonvaccinated patients [20]. There were no significant association between oxygen delivery mode and vaccine status. Most of the patients both vaccinated and nonvaccinated were on intermittent Non-invasive ventilation and non-rebreathing mask. ($p = .06$). There was a significant difference among vaccinated (8.55 ± 3.21) and nonvaccinated (11.55 ± 4.56) $p < .041$ in duration of ICU stay.

Table 2- CT score and vaccine status

		vaccine status		Total
		No dose	Either 1 or 2 dose	
CT score	Mild	2	3	5
	Moderate	41	29	70
	Severe	197	35	232
Total		240	67	307

p value $< .001$

The above results are very much promising and vaccinated people had less mortality. We have to use our precious time to vaccinate all eligible people with two doses. With children still unvaccinated and many adults yet to receive the second dose a mutant variant at this time will result in rapid transmission and high transmissibility in this population. Mutations becoming inevitable long-term preparations and strategic planning to live with covid pandemic is essential. India has been successful in vaccinating more than 100 crore vaccine doses but these are single dose and not complete two dose which could be effective in fighting the new strain

Limitations

This study was conducted at a single-centre, and only one type of vaccine covishield was researched. Only patients with relatively severe COVID-19 pneumonia were hospitalized during this period. Moreover, all vaccinated patients were not hospitalised. Patients age less than 18 though positive were excluded. Post Vaccination seroconversion which is a surrogate marker for vaccine efficacy could not be done because of limited resources.

Conclusion

We conclude that single dose of covishield is effective against SARS-CoV-2 infection 14 days post vaccination with the first dose. Immunization with the second dose should be achieved to attain the total protection against Covid 19. With new variants and new waves of infection anticipated we should act quickly and efficiently to improve the vaccination drive. However, the risk of infection cannot be eliminated, highlighting the need for non-pharmaceutical interventions such as face mask, hand hygiene and social distancing.

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