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Vaccination Status And Covid-19 Infection Severity And Outcome: A Retrospective Hospital Based Study

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Abstract

Background and Objectives: There have been extensive clinical trials about COVID-19 vaccination efficacy which may not be translated into real-world performance. This study tries to find if vaccination status reverberates with in-hospital severity and outcome of COVID-19 infection.

Methods: The present retrospective study included 671 admitted COVID-19 patients in a Bengaluru tertiary care hospital. The patient's data concerning medical history, laboratory findings, severity and outcome were extracted from their medical records for subsequent evaluation, interpretation, and association.

Results: The 671 patients included in the study had a male preponderance with a mean age of 52.2 (± 18.54) years. A total of 123 (18.3%) patients were partially vaccinated and 386 (57.5%) were fully vaccinated. Overall, 379 (56.4%) patients had co-morbidities and 86(12.8%) died. Among those fully vaccinated, there was 8% (31/386) mortality while it was 19.1% (31/162) among the unvaccinated ($p<0.001$). Among unvaccinated and partially vaccinated, 22.2% and 20.3% (36/162; 25/123) had severe infection while only 10.1% (39/386) ($p<0.001$) among fully vaccinated had severe infection. Out of the 509 vaccinated, 379 (74.4%) had been vaccinated with COVISHIELD®, 129 (25.3%) with COVAXIN and 1 with Pfizer. Mortality was 8.9% (26/292) among fully vaccinated with COVISHIELD, and 5.4% (5/93) among fully vaccinated with COVAXIN.

Interpretation and Conclusion: Vaccination with two doses was associated with less severe infection and less mortality among hospitalized patients with COVID-19 infection compared to partially vaccinated and unvaccinated patients.

Keywords: Covid-19, Vaccination, Mortality

Introduction

The seventh human coronavirus (SARS-CoV-2), causing the clinical syndrome COVID 19, was initially described in the Hubei province of China during a pneumonia epidemic in January 2020[1].

The origin of the virus has been extensively probed amidst speculations of laboratory manipulations. Mutations in the spike protein receptor binding domains have increased the affinity of SARS-CoV-2 with ACE2 receptor on human cells compared to other coronaviruses, but are not consistent with purposefully alterations to any known viral backbones. These and other mutations can also be explained by zoonotic transfer theories, but it is currently impossible to validate them[2].

The virus mainly affects the respiratory tract, where ACE2 receptors are abundant. Post infection,

treatment with remdesivir, favipiravir, arbidol and other drugs have been found effective depending on the clinical scenario. However, contradictory results of various popular drugs drastically limit wide application[3].

A cornerstone of the global approach to curb the COVID-19 pandemic was vaccine development. The process began as soon as the genetic sequence of SARS-CoV-2 was published on 11th January 2022 and was able to enter human clinical testing by 16 March 2020. Platforms explored included nucleic acids, virus-like particles, viral vectors, live attenuated virus and inactivated virus[4].

In India, the National Expert Group on Vaccine Administration for COVID-19 (NEGVAC), was constituted by the Ministry of Health and Family Welfare for guidance on all aspects of COVID-19 vaccination in mid-2020 and the vaccination drive began on January 16, 2021. At the inception of vaccination drive, 2 major vaccines: Covishield (Oxford-AstraZeneca vaccine, the name designated by India; an adenovirus vaccine carrying SARS-CoV-2 S protein) and Covaxin (Bharat Biotech, India, an indigenous inactivated SARS-CoV-2) were approved. Later, other vaccines such as Sputnik V were approved by the DGGI[3].

According to WHO, as of 28th November 2022, the SARS-CoV-2 virus has caused 637,404,847 human infections worldwide and 6,608,893 deaths. 12,959,275,260 vaccine doses have been administered with **4,992,546,551** people being completely vaccinated. In India, 159 doses have been administered per 100 population[5].

All vaccines have been subjected to extensive pre-clinical and clinical trials. However, whether their efficacy in terms of disease severity and outcome in an infected patient extends into the real world is still under evaluation.

Data from the National Clinical Registry for COVID-19 between November 2021 and January 2022 shows a steep rise in the number of cases in a significantly vaccinated population, making it an ideal time and person distribution for evaluation of vaccination performance[6].

This study tries to find if vaccination status reverberates with in-hospital severity and outcome of COVID-19 infection and compares COVAXIN with COVISHIELD.

Methodology:

This was Retrospective observational study conducted among patients admitted under medicine department between Dec 2021 to Feb 2022 at a Tertiary care hospital, Bangalore,

Karnataka, India. Approval and clearance were obtained from the institutional ethics

committee. The study included patients aged ≥ 18 years of both genders, with COVID-19 infection diagnosed by RT-PCR technique using ABI/Thermofischer - Taqppath technique. Case record form with follow-up chart was used to record the demographic data, vaccination status including type, number of doses, and dates, comorbidities, clinical features, duration and outcome of the disease. Disease severity was classified into asymptomatic, mild, moderate and severe based on oxygen saturation, need for ventilatory support and ICU admission.

Statistical Analysis

SPSS (Statistical Package For Social Sciences) version 20. (IBM SPASS statistics [IBM corp. released 2011] was used to perform the statistical analysis

Data was entered in the excel spread sheet. Descriptive statistics of the explanatory and outcome variables were calculated by mean, standard deviation for quantitative variables, frequency and proportions for qualitative variables.

Inferential statistics like

Chi-square test was applied to associate the qualitative variables.

ANOVA test was applied to compare the lab parameters among the groups (based on severity).

The level of significance is set at 0.05.

Results:

Demographics And Comorbidities:

The 671 patients included in the study had a male preponderance with a mean age of 52.2 (± 8.54) years.

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Table 1: Gender Distribution:

Gender	Frequency	Percent
Females	273	40.7
Males	398	59.3
Total	671	100.0

Table 2: Age Distribution:

Age groups	Frequency	Percent
13 to 30	109	16.2
31 to 40	82	12.2
41 to 50	107	15.9
51 to 60	128	19.1
61 to 70	130	19.4
> 70	115	17.1
Total	671	100.0

Overall, a total 379 (56.4%) patients had comorbidities, including hypertension (32.2%), diabetes mellitus(25.8%), chronic kidney disease (11.9 %), ischemic heart disease (7.3%), bronchial asthma (3%), pulmonary tuberculosis (3%), cerebrovascular accident and COPD.

Vaccination Status:

The study population was classified based on vaccination into 3 categories:

1. Unvaccinated: Those who have not received any dose of and COVID-19 vaccination (24.1%).
2. Partially vaccinated: Those who have received at least one dose of any WHO approved COVID-19 vaccination (18.3%).
3. Fully vaccinated: Those who have completed the last dose of a primary series of COVID- 19 vaccination (57.5%).

Severity:

The study population was classified based on clinical severity of infection into: Asymptomatic - 20 (3%)

Mild infection: Upper/lower respiratory tract infection without oxygen requirement - 356 (53.1%)

Moderate infection – Lower respiratory tract infection requiring oxygen - 195 (29.1%)

Severe infection – Lower respiratory tract infection requiring ventilation (invasive/noninvasive) - 100 (14.9%)

Majority (53.1%) of the patients had mild infection.

Outcome:

The study population had the following outcomes overall:

Death: 86 patients (12.8 %)

Discharge: 583 patients (86.9 %) Discharge against advice: 2(0.3%)

Vaccination Status And Severity:

Among those fully vaccinated, there was 8% (31/386) mortality while it was 19.1% (31/162) among the unvaccinated ($p<0.001$). Among unvaccinated and partially vaccinated, 22.2% and 20.3% (36/162; 25/123) had severe infection while

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only 10.1% (39/386) (p<0.001) among fully vaccinated had severe infection

Table 3: Association Of Vaccination Status With Severity

Severity		Vaccination status			Total
		Fully vaccinated	Not vaccinated	Partially vaccinated	
Asymptomatic	Count	12	2	6	20
	%	3.1%	1.2%	4.9%	3.0%
Mild	Count	235	63	58	356
	%	60.9%	38.9%	47.2%	53.1%
Moderate	Count	100	61	34	195
	%	25.9%	37.7%	27.6%	29.1%
Severe	Count	39	36	25	100
	%	10.1%	22.2%	20.3%	14.9%
Total	Count	386	162	123	671
	%	100.0%	100.0%	100.0%	100.0%
Chi-square value- 34.29					
p value- 0.001*					

Table 5: Association Of Vaccination Status With Outcome

Outcome		Vaccination status			Total
		Fully vaccinated	Not vaccinated	Partially vaccinated	
DAMA	Count	0	2	0	2
	%	0.0%	1.2%	0.0%	0.3%
DEATH	Count	31	31	24	86
	%	8.0%	19.1%	19.5%	12.8%
DISCHARGE	Count	355	129	99	583
	%	92.0%	79.6%	80.5%	86.9%
Total	Count	386	162	123	671
	%	100.0%	100.0%	100.0%	100.0%
Chi-square value- 25.24					
p value- 0.001*					

*significant

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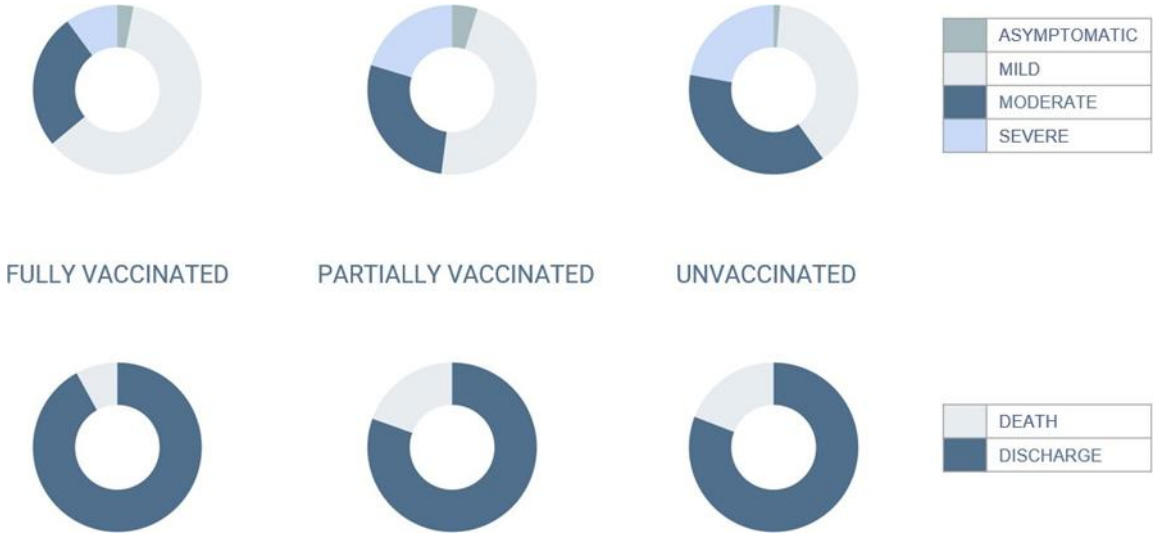

Out of the 509 vaccinated, 379 (74.4%) had been vaccinated with COVISHIELD®, 129 (25.3%) with COVAXIN and 1 with Pfizer. Mortality was 8.9% (26/292) among fully vaccinated with COVISHIELD, and 5.4% (5/93) among fully vaccinated with COVAXIN

Table 6: Association Of Vaccination Status With Severity Based On The Type Of Vaccine

TYPE	Severity		Vaccination status		Total	Chi-square value	p value
			Fully vaccinated	Partially vaccinated			
COVAXIN	Asymptomatic	Count	2	0	2	2.76	0.42
		%	2.2%	0.0%	1.6%		
	Mild	Count	59	21	80		
		%	63.4%	58.3%	62.0%		
	Moderate	Count	27	9	36		
		%	29.0%	25.0%	27.9%		
	Severe	Count	5	6	11		
		%	5.4%	16.7%	8.5%		
	Total	Count	93	36	129		
		%	100.0%	100.0%	100.0%		
COVISHIELD	Asymptomatic	Count	9	6	15	9.55	0.022*
		%	3.1%	6.9%	4.0%		
	Mild	Count	176	37	213		
		%	60.3%	42.5%	56.2%		
	Moderate	Count	73	25	98		
		%	25.0%	28.7%	25.9%		

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	Severe	Count	34	19	53		
		%	11.6%	21.8%	14.0%		
	Total	Count	292	87	379		
		%	100.0%	100.0%	100.0%		
PFIZER	Asymptomatic	Count	1		1	-	-
		%	100.0%		100.0%		
	Total	Count	1		1		
		%	100.0%		100.0%		

Table 7: Association Of Vaccination Status With Outcome Based On The Type Of Vaccine

TYPE	Outcome		Vaccination status		Total	Chi-square value	p value
			Fully vaccinated	Partially vaccinated			
COVAXIN	Death	Count	5	6	11	2.91	0.087
		%	5.4%	16.7%	8.5%		
	Discharge	Count	88	30	118		
		%	94.6%	83.3%	91.5%		
	Total	Count	93	36	129		
		%	100.0%	100.0%	100.0%		
COVISHIELD	Death	Count	26	18	44	7.96	0.004*
		%	8.9%	20.7%	11.6%		
	Discharge	Count	266	69	335		
		%	91.1%	79.3%	88.4%		
	Total	Count	292	87	379		
		%	100.0%	100.0%	100.0%		
PFIZER	Discharge	Count	1	0	1	-	-
		%	100.0%	0	100.0%		
	Total	Count	1	0	1		
		%	100.0%	0	100.0%		

Discussion:

This study demonstrated the impact of COVID 19 vaccination with Covishield™ and Covaxin, in the real-world scenario, in a predominantly vaccinated population during the Indian third wave of COVID-19 infection during the months of November-January 2022. The paramount finding of this study was the significant decrease in both severity of infection and mortality in fully vaccinated patients compared to partially or unvaccinated patients. Since early 2021, two chief vaccines are available in India, i.e Covaxin and Covishield. These vaccines were distributed as liquid preparations in multidose vials by the government of India and were widely available by midyear.[7]

Although many previous studies had established the efficacy of vaccination in reducing mortality

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complications and infection severity, the effectivity against variant stains of corona virus, such as the omicron variant was a matter of curiosity at the time of commencement of this study. The infections occurring during the latter half of 2021 and early 2022 in India were largely consisting of the omicron variant.[8]

A systematic review by Ibrahim Mohammed et al. concluded that despite of the high effectiveness of the newly developed COVID-19 vaccines in reducing the rates of infections, hospitalizations, severity and mortality, more efforts are required to test the efficacy/effectiveness of these vaccines against the other newly emerging variants.[9]

A similar detailed in-hospital study was conducted by Abhilask KPP et al in April and March 2021 during the delta variant predominant second wave in India. This study also showed a graded benefit of vaccination in reducing severity and mortality in both Covaxin and Covishield groups.[10]

Another study done on Indian population during the second wave by J. Muthukrishnan et al. showed similar benefit of vaccination in-hospital in a population with significant comorbidities. This study included 1168 patients but the population was not largely vaccinated.[11]

A stand out point compared to other studies is the failure of partial vaccination to provide much benefit in mortality or severity reduction as opposed to complete vaccination, which provides definite benefit. The mortality rate in both partially vaccinated and unvaccinated hovered around 19%, while it was only 8% in the fully vaccinated group. Similarly, severe infection was seen in about 20% of the unvaccinated and partially vaccinated groups as opposed to just 10% in the fully vaccinated group. This observation highlights the importance of completing the last dose of the primary series of any COVID 19 vaccination schedule.

Recently, there has been focus on factors contributing to vaccination hesitancy by public health workers both in India, and globally. A meta-analysis by Fajar et al analyzed 56 articles and concluded that multiple socio-economic factors were pivotal in vaccine hesitancy. They include female sex, unemployment, living alone or in a household with five or more individuals, poor educational status, and considering COVID-19 vaccines to be unsafe. In contrast, living with children at home, maintaining physical distancing norms, having ever tested for COVID-19, and having a history of influenza vaccination in the past few years were associated with less vaccine hesitancy.[12]

Current challenges in the war against COVID-19 include minimizing vaccine hesitancy as well as tackling adverse reactions to these vaccines.

Common symptoms post vaccination are localized pain and swelling at the injection site, fever, headache, myalgia, and chills. A few cases of thrombosis, notably CVT, are mostly seen with the adenoviral vector vaccines. Other adverse effects such as myocarditis, glomerular diseases, and cutaneous eruptions are seen with the mRNA vaccines. Most vaccination reactions peak within the first 6 weeks.[13]

Although our study shows a lower mortality in the Covaxin group compared to Covishield, the sub groups were dissimilar and hence statistical significance could not be derived.

However, a study by Suri et al conducted on a group of 353 patients concluded that there was no difference in in hospital mortality between recipients of the two vaccines. Furthermore, there was no difference in severity of infection need for mechanical ventilation or duration of stay. [14]

The limitations of this study include the non-inclusion of immunosuppression and comorbidities altering the immune response to vaccination. Prior infection with COVID-19 and persistent immune response was not considered. The impact of booster doses, if any, were not considered. Time elapsed since last dose of vaccination was not analysed. A large proportion of in-hospital patients were asymptomatic during the time of study due to government quarantine policy that prevailed at the time of study, but this maybe not be replicated temporally.

Conclusion:

Among hospitalized COVID-19 patients, complete vaccination with either Covishield™ or Covaxin® positively impacted mortality and severity of illness as compared to partial vaccination or no vaccination. Partial vaccination did not confer much benefit.

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