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Comparison of Severity of COVID-19 Infections between Vaccinated and Unvaccinated Patients with Comorbidities in the Third Wave

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Abstract

Introduction: *Vaccination has proven to be the most effective weapon in controlling the COVID-19 pandemic. The present study was undertaken to compare the severity of infection in vaccinated and unvaccinated COVID-19 patients with comorbidities during third wave in India.*

Materials and Methods: *The present retrospective study included 671 patient admitted in a Bengaluru tertiary care hospital, categorized in to two groups : the vaccinated and the unvaccinated. These groups were further classified into subgroups based on severity of infection and comorbidities [DM, HTN, IHD, CKD]. The patient's data concerning medical history, clinical manifestations, laboratory findings, and radiological parameters were extracted from their medical records for subsequent evaluation, interpretation, and association among the groups.*

Results: *Out of the 671 samples, mean age was 52yrs, 398(59.3%) were males and 273(40.7%) were female patients. Majority of the patients were aged between 51-70yrs. It was observed that 386 were fully vaccinated,162 were not vaccinated and 123 were partially vaccinated. Diabetic and Hypertensive patients with completed vaccination status were more likely to have asymptomatic or mild-moderate disease compared to the unvaccinated or the partially vaccinated groups In the subgroups of patients with CKD and IHD, it was found that unvaccinated patients had a higher percentage of severe disease compared to the completely vaccinated groups. This was statistically proved to be significant across the 4 co morbidities: Diabetes, Hypertension , Ischaemic Heart Disease [IHD] and Chronic Kidney Disease [CKD].*

Conclusion: *COVID-19 vaccines are effective at substantially mitigating the severity of the infection even in individuals with comorbidities, who are more susceptible for worse outcomes. Widespread vaccination will remain a major goal to prevent future breakouts and to prevent severe infections.*

Introduction

In December 2019, a new flu-like virus causing atypical pneumonia emerged, affecting many individuals in the city of Wuhan, China. The syndrome caused by this virus, later recognized as coronavirus disease 2019 (COVID-19),[1] reached pandemic levels wreaking havoc throughout the globe. COVID-19 cases have been classified as mild, moderate, and severe or critical. In its mild form, the symptoms are a cough and fever, while imaging shows no signs of lung inflammation. A case is classified as moderate if the patient has a fever, respiratory tract symptoms, and imaging shows visible lung inflammation. Severe cases of COVID-19 include adults with any of the following: shortness of breath (respiratory rate of >30 breaths per minute), oxygen saturation <93% at rest, or arterial oxygen partial pressure <300 mmHg.

The overall case fatality rate due to COVID 19 was 10%. Compared to the first and the second wave, Omicron variant, which was responsible for third wave, has increased transmissibility, severe disease course, reduced effectiveness of treatments. However, we had a new weapon to combat the virus this time- the vaccine. The process of vaccine development 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 as early 16 March 2020. Extensive pre-clinical and clinical trials were carried out before the vaccine was released.

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. With vigorous public health efforts, India boasts upto 90% of its adult population completely vaccinated against the COVID-19 virus.Translation of these numbers as vaccine efficacy in the real-world scenario is yet to be evaluated completely.

The vaccine can estimatedly protect four out of every five fully vaccinated individuals from contracting SARS CoV-2 infection. [9] This has already been established in multiple studies and reviews. However, whether the vaccine can curb severe disease in patients with breakthrough infections is still a subject of much debate. No vaccine is 100% effective and 'Breakthrough cases' are expected, especially before population immunity reaches sufficient levels to further decrease transmission [10]. In the Pan-India cross-sectional COVAT study, Breakthrough infections were noted in 5.5% of Covishield and 2.2% of Covaxin recipients A good time to study the effects of the vaccine in this area is the third wave as shown by the Data from the National Clinical Registry for COVID-19 between November 2021 and January 2022 where a steep rise in the number of cases in a significantly vaccinated population has been noted, making it an ideal time and person distribution for evaluation of vaccination performance. [8]

This study has targeted the most vulnerable population – the patients with past history of comorbidities. The efficacy of the vaccine in breakthrough infections in such patients has been studied with respect to severity of infection.

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, 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.

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 (3.2%), diabetes mellitus(25.8%), chronic kidney disease (11.9 %), ischemic heart disease (7.3%), bronchial asthma (3%), pulmonary tuberculosis (3%), cerebrovascular accident and COPD. 214 of these patients had multiple comorbidities.

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%)

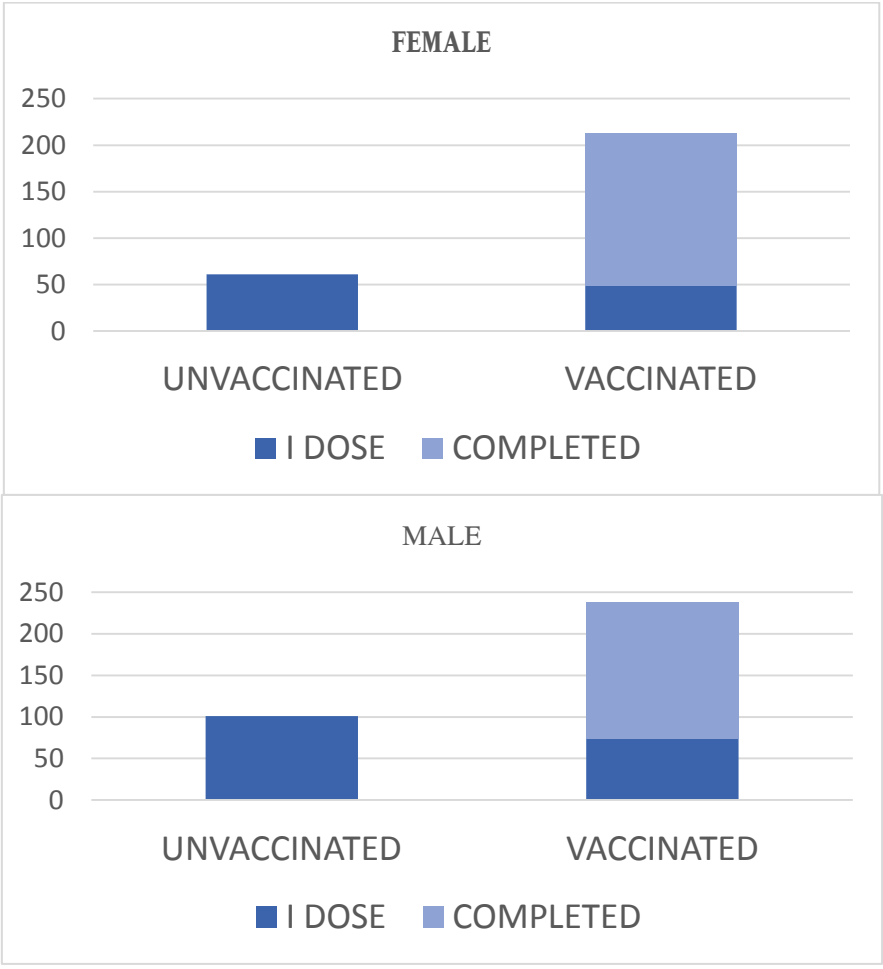
Mild infection: Upper/lower respiratory tract infection without oxygen requirement - 356 (53.1%)

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

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

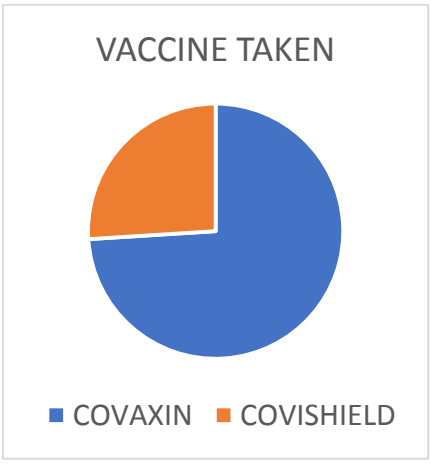
Majority (53.1%) of the patients had mild infection

Vaccination Status in Males and Females



Type of Vaccine Taken

74% of the study population i.e. 496 individuals had taken the COVAXIN vaccine while the remaining 26% were vaccinated with COVISHIELD.



Vaccination Status with Severity of Infection

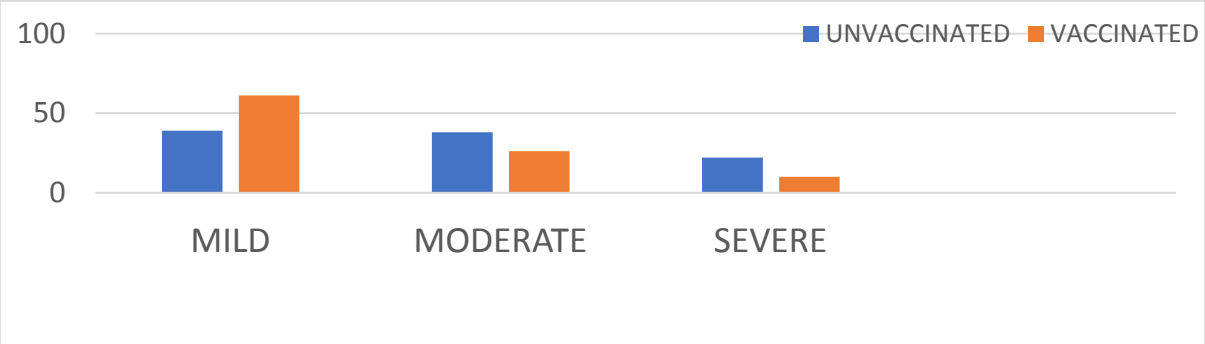


Table 3: Association of Vaccination Status with Severity

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

It was noted that 22.5% patients who were unvaccinated suffered severe infections whereas 10.1% of completely vaccinated patients suffered severe infections. 60.9% patients with full vaccinated status were afflicted with mild infection while only 38% of the unvaccinated group suffered mild variety of COVID.

Further, 4 comorbidities were chosen- Diabetes Mellitus, Hypertension, Chronic kidney disease and Ischaemic heart disease. They were subdivided according to severity and vaccination status

Diabetes Mellitus

		Fully vaccinated	Not vaccinated	Partially vaccinated			
Asymptomatic	Count	2	0	0	2	18.78	0.005*
	%	2.1%	0.0%	0.0%	1.2%		
Mild	Count	51	18	6	75		
	%	54.3%	34.6%	22.2%	43.4%		
Moderate	Count	26	29	14	69		
	%	27.7%	55.8%	51.9%	39.9%		
Severe	Count	15	5	7	27		
	%	16.0%	9.6%	25.9%	15.6%		
Total	Count	94	52	27	173		
	%	100.0%	100.0%	100.0%	100.0%		

Mild [54%] and moderate [27.7%] disease was found to be more common in patients with the fully vaccinated Diabetics afflicted with COVID-19. This was found to be statistically significant when compared to the unvaccinated group.

Hypertension

		Fully vaccinated	Not vaccinated	Partially vaccinated			
Asymptomatic	Count	1	0	1	2	17.68	0.005*
	%	.9%	0.0%	2.6%	.9%		
Mild	Count	58	24	12	94		
	%	54.2%	34.3%	30.8%	43.5%		
Moderate	Count	30	36	14	80		
	%	28.0%	51.4%	35.9%	37.0%		
Severe	Count	18	10	12	40		
	%	16.8%	14.3%	30.8%	18.5%		
Total	Count	107	70	39	216		
	%	100.0%	100.0%	100.0%	100.0%		

It was found in our study that mild disease was more prevalent in the fully vaccinated group while the moderate severity of disease was more prevalent in the unvaccinated population. This was found to be statistically significant.

Ischaemic Heart Disease [IHD]

		Fully vaccinated	Not vaccinated	Partially vaccinated			
Asymptomatic	Count	0	0	0	0	9.52	0.049*
	%	0.0%	0.0%	0.0%	0.0%		
Mild	Count	21	3	0	24		
	%	60.0%	27.3%	0.0%	49.0%		
Moderate	Count	13	6	3	22		
	%	37.1%	54.5%	100.0%	44.9%		
Severe	Count	1	2	0	3		
	%	2.9%	18.2%	0.0%	6.1%		
Total	Count	35	11	3	49		
	%	100.0%	100.0%	100.0%	100.0%		

The unvaccinated cohort in our study who were also suffering from IHD had a statistically significant preponderance to have severe disease [18.2%] when compared with the completely vaccinated group [2.9%].

Chronic Kidney Disease

It was statistically evident from our study that patients with chronic kidney disease had a higher tendency to suffer from severe COVID when they were not vaccinated [36%] . Only 7.1% patients with chronic kidney disease had severe disease.

Discussion

This study demonstrated the impact of COVID 19 vaccination in the real-world scenario, in a predominantly vaccinated population during the Indian third wave of COVID-19 infection which occurred in the months of November-January 2022. The specific populations that were picked here were the patients with comorbidites- Diabetes, Hypertension, IHD and CKD. In individuals with COVID-19, the presence of co-morbidities (both cardiometabolic and other) is associated with a higher risk of severe COVID-19 and mortality. [6]With this knowledge in the background, vaccination drives prioritized these groups over the general population. Hence, the effect of vaccination in these patients was of utmost interest.

The paramount finding of this study was the significant decrease in severity of infection in fully vaccinated patients compared to unvaccinated patients. This was in the form that mild to moderate degree of infection were more prevalent in diabetics and hypertensives in the patients with complete vaccination status while in patients with CKD and IHD, severe disease was significantly higher in unvaccinated patients. This establishes the robustness of immunization in special populations.

A study by Wan EY et al conducted in both in-hospital and outpatient settings among COVID patients with diabetes demonstrated vaccine effectiveness was relatively high with respect to severity, all-cause mortality and post infection cardiovascular disease. They studied the effect of booster doses as well.

Another study done by Swamy S et al in Washington, USA showed Data for the BNT162b2 vaccine that indicated that the vaccine is highly efficacious in patients with hypertension at 94.6%. [11]

This study has put COVAXIN and COVISHIELD into focus. A study done by Dagan N et al in Israel evaluated the effectiveness of the BNT162b2 mRNA Covid-19 Vaccine in a setting of mass vaccination.[12] The cumulative outcome of documented covid infections, symptomatic infections, hospitalizations ,severe infections and deaths due to breakthrough infections were taken into account. They found that the vaccine was consistently effective across various specific subpopulations, potentially slightly lower effectiveness in persons with multiple coexisting conditions.

The limitations of the above study were that 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. The status of these comorbidities with parameters such as HbA1c, blood pressure, need for maintenance hemodialysis and heart failure, if any, were not taken into account. The effect of combination of these conditions could also not be studied.

Conclusion

Vaccines are an important tool in protecting the patients with Diabetes mellitus, Hypertension, CKD and IHD who are especially susceptible to severe infection. Widespread vaccination and timely boosters should be targeted for controlling future COVID-19 breakouts.

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