EFFECTIVENESS OF VACCINATION IN PREVENTING SEVERE SARS COV-2 INFECTION IN SOUTH INDIA-A HOSPITAL-BASED CROSS-SECTIONAL STUDY

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Abstract: Establishing concrete evidence on the effect of vaccination on the severity of SARS CoV-2 infections in real-world situations is the need of the hour. This study aims to estimate the effectiveness of Covid 19 vaccines in preventing the new and severe SARS CoV-2 infections. The design is cross-sectional study. **Material and Methods:** We did this cross-sectional study among the consecutive 2027 SARS Cov-2 infected patients admitted in the Covid 19 wards of a tertiary care hospital from May 7, 2021, to October 7, 2021, during the second wave of the Covid 19 pandemic. Information on basic demographic variables, RT PCR status, vaccination status, outcome and clinical severity of illness were obtained from the electronic hospital patient records. **Results:** Only 4% of the study participants had prior vaccination. The type of vaccine and number of doses didn't have any protective effect against the new SARS CoV-2 infection and breakthrough infection. Fully vaccinated RTPCR positive patients had an 82% reduction in the need for ICU admission (OR 0.09; AOR 0.18, CI (0.04 to 0.8), $P <0.05$) and a non-significant 79% reduction in mortality (OR 0.19; AOR 0.21, CI (0.04 to 1.1) $P>0.05$). **Conclusion:** Vaccination doesn't protect against new SARS Cov-2 infection and breakthrough infection however significant protection was documented against severe SARS Cov-2 infection. The protective effect shown by the vaccines in preventing the severe form of SARS Cov-2 infection among fully vaccinated patients was 82%.

INTRODUCTION

The impact caused by the Novel SARS-CoV-2 virus on global health is indescribable. Vaccination drive is one of the most imperative strategies ratified to combat the deadly pandemic. Eradication of the Covid19 may be too aspirational a goal given the current situation; but elimination of Covid 19 is still a realistic goal. Israel has achieved an all-time low level of infections of SARS-CoV-2 with high vaccination coverage[1]. India being the pharmaceutical hub; there are 8 vaccines in the pipeline under various phases of the clinical trial and 2 vaccines – Covishield and Covaxin are in wide usage[2]. Covishield, produced by Serum Institute of India in synergy with Oxford University and Pharmaceutical giant Astra Zeneca uses a non-replicating adenovirus viral vector that infects chimpanzees given in 2 doses 84 days apart. The efficacy of the vaccine was found to be 76% after the first dose. If the interval between the first and second dose was extended to 12 weeks or more the efficacy rose to 91.6%[3]. Covaxin, a domestic vaccine developed in the country by Bharat Biotech in collaboration with the Indian Institute of Medical Research (ICMR) and subsidiary National Institute of Virology (assisted by isolating virus sample) is an inactivated vaccine given 28 days apart with a vaccine efficacy of 81%[4].

Vaccine efficacy is defined as reduced risk of infection or disease among vaccinated individuals resulting from vaccination in carefully controlled circumstances; estimated from randomized clinical trials. Vaccine effectiveness is reduced risk of infection or disease among vaccinated individuals attributed to vaccination in real-world conditions; estimated from observational (non-randomized) studies. Gauging COVID-19 vaccine performance in the real world is crucial. Several factors like cold chain management during transportation and storage, completing dosing schedule, the inclusion of the general population (as people enrolled in a clinical trial are many times young and healthy) have a bearing on real-world vaccine effectiveness[5].

The national covid vaccination program of India was launched on 16 January 2021 in the country with the first phase covering Health Care workers and frontline workers. Vaccine hesitancy is one of the top ten global health threats reported by the World health organization which threatens the progress made against vaccine-preventable diseases[6]. In the state of Tamil Nadu, though the vaccine coverage has improved a lot, the proportion of fully vaccinated people is still low[7]. With high vaccine hesitancy among the population, providing concrete evidence on the effect of vaccination on the severity of the disease has become crucial and need of the hour. Hence this study was done to analyse effectiveness of vaccine in preventing severe SARS CoV-2 infection as there is a significant dearth of such studies in our country.

Objective:

1. To estimate the occurrence of new SARS CoV-2 infections following Covid vaccination among the patients admitted in Covid 19 wards in a tertiary care hospital, South India.

2. To find out the effectiveness of Covid vaccination in preventing the severe SARS CoV-2 infections among the patients admitted in Covid 19 wards in a tertiary care hospital, South India.

MATERIAL and METHODS

Study setting: Triage Centre and Covid 19 ward of a tertiary care hospital, South India

Study design: Cross-sectional study

Study period: May 7, 2021, to October 7, 2021

Study population: Inpatients admitted in Covid 19 wards

Inclusion criteria: All patients with RTPCR test positive for SARS Cov-2 infection (Aged ≥ 13 years) admitted in Covid 19 wards during the above said period were included.

Exclusion criteria: Children (aged <13 years) were excluded from the study population as vaccination for them wasn't started yet. Patients with incomplete data on outcome measured were excluded from the study.

Sampling method: Consecutive sampling; all the eligible consecutive patients admitted in the covid 19 wards were included.

Sample size: Not applicable.

Ethical committee approval: Institutional research ethics committee approval was got. (Tirunelveli medical College Institutional research ethics committee has approved the study on 19.08.2021. Approval number REF NO:1975/CM /2021). Verbal consent was taken from the participants.

Study procedure: We did this cross-sectional study among the consecutive adult inpatients admitted in the Covid 19 wards of a tertiary care hospital, South India in the above said period. An Electronic patient record database had been developed and maintained by the hospital Covid control room and the required study variables were extracted from the database. After getting approval from the Institutional ethics committee, the following variables were collected; Name, age, sex, phone number, address, district, presence of symptoms, history of comorbid conditions, RT PCR status, SPO2, Respiratory rate, outcome, vaccination status, type of vaccine taken, number of doses, date of first positive and the difference between the date of RT PCR positive and date of vaccination. Self-reporting of vaccination status was confirmed through verification in the COWIN portal. The clinical severity of illness was categorized based upon the Respiratory Rate and Spo2 level measured at the time of admission.

Clinical guidelines for the management of Covid 19 issued by the Ministry of Health and family welfare, Government of India was followed for disease classification as follows[8]:

Mild: SpO2 >94 and RR<24/min; Moderate: SpO2 90 - 94 and RR 24 - 30 /min

Severe: SpO2 < 90 and RR >30 /min.

World health organization definition for SARI (severe acute respiratory illness infection) was used. SARI is defined as a hospitalized person with an acute respiratory infection, with a history of fever or measured fever of ≥ 38°C and cough with onset within the last 10 days[5]. Vaccine breakthrough infection is defined as the detection of SARS-CoV-2 RNA or antigen in a respiratory specimen collected from a person ≥14 days after they have completed all recommended doses of COVID-19 vaccine[9]. Vaccine effectiveness was calculated using the formula 1-AOR[5].

Data analysis: Data entry was done with Microsoft Excel and data analysis was done with SPSS 23 Version. Frequencies and proportions were calculated as appropriate. Means, Range and standard deviation were calculated for quantitative variables. The difference between the proportions was calculated using the Chi-Square test. Differences between more than two proportions were calculated using the Chi-Square trends. Multi variate logistic regression was done for adjusting the confounders.

RESULTS

A total of 5291 patients have been admitted in Covid 19 wards during the above said period. After excluding patients with incomplete data about the main outcome studied (absent Spo2; n=636) and children aged less than 12 years (=90) a total of 4565 patients were eligible and among them 2027 patients were RTPCR positive. The majority of the patients were male (56%). The majority of the patients belonged to the age group of 61-70 years (24.6%) followed by the 51-60 years (24.2%) age group. The mean age of the study population was 54.3 years and the standard deviation was 16.1; the Median was 56 years.

Effectiveness of Covid 19 vaccine in preventing new SARS CoV 2 infection: Our study didn't find any protective effect of vaccination against new COVID 19 infections. Type of vaccine nor number of doses has any effect on new infection. Females (1.2 times), people vaccinated with at least one dose of Covid 19 vaccine (1.8 times) and people who had 2 doses (2 times) and people who had Covaxin (2.3 times) had higher odds of becoming infected with SARS CoV 2 virus and they were statistically significant also (p<0.05). However, after multiple logistic regression analyses, none of them was found to be statistically significant [Table 1].

Effectiveness of Covid 19 vaccine in preventing breakthrough SARS CoV 2 infection: Out of the 52 patients who had 2 doses of vaccines, the data on days between the second dose of vaccination and date of RT PCR positive was available only for 45 patients. 23 of them (51%) had a breakthrough infection (RT PCR positive after 14 days of vaccination). Sex, age, presence of comorbid status and type of vaccine were considered for cross-tabulation. People vaccinated with Covaxin (OR 4.1 times, AOR 5.7(95% CI 1.3 to 26)) had higher odds of becoming infected with the SARS CoV 2 virus after 14 days of vaccination and it was statistically significant also (p<0.05) [Table 1].

Effectiveness of Covid 19 vaccine against severe SARS CoV-2 infection: Males (1.3 times), those aged more than 56 years (2 times) and patients with co-morbidity (1.6 times) have higher odds of requiring ICU care. Males (1.3 times), those aged more than 56 years (2.2 times) and patients with co-morbidity (3 times) have higher odds of dying and they were statistically significant(p<0.05). All the above factors were considered for multivariate logistic regression. The risk was augmented significantly for the baseline variables. Males had only higher odds of ICU admission need (AOR 2.9 (95% CI 1 to 8.8)) not for mortality. Patients with co-morbidity had significantly higher odds of ICU admission need (AOR 5.8 (95% CI 1.8 to 18.6) and mortality risks (AOR 10.3(95% CI 2 to 52.6)).

Partially vaccinated RTPCR positive patients had a 60% reduction in the need for ICU admission and 30% fewer odds of dying. Fully vaccinated RTPCR positive patients had a 91% reduction in the need for ICU admission and 81% fewer odds of dying; both were statistically significant(p<0.05). However, after logistic regression analysis, fully vaccinated RTPCR positive patients had an 82% significant reduction (AOR 0.18, 95% CI (0.04 to 0.8)) in the need for ICU admission but the reduction shown in mortality (AOR 0.21, 95% CI (0.04 to 1.1)) had become non-significant. The protective effect shown by the vaccines in preventing a severe form of SARS Cov-2 infection among fully vaccinated patients was 82%.

The Covaxin vaccine seemed to be offering significantly higher protection against severe SARS Cov-2 infection as compared to the Covishield vaccine. Patients with Covishield vaccination had 67% less ICU admission need and 40 % less risk of death whereas those vaccinated with Covaxin had an 85% reduction (OR 0.15, AOR 0.85; (95% CI 0.2 to 3.3) in the need for ICU admission and 60% fewer deaths (OR 0.4, AOR 1.3; (95% CI 0.3 to 6.1)). However, after logistic regression analysis, it became not significant [Table 2].

Table 1. Effectiveness of Covid 19 vaccine in preventing new/breakthrough SARS CoV 2 infection

I. Occurrence of new SARS CoV 2 infection (n=4565)

	Category	RT PCR Positive (n=2027)	RT PCR Negative (n=2538)	Odd's ratio (95%CI)	Adjusted OR (95%CI)
Sex	Male	1092(42.6%)	1471(57.4%)	0.9 (0.8 to 0.9) *	0.6 (0.3 to 1.2)
	Female	935(46.7%)	1067(53.3%)		
Age >56 years	Yes	996(43.9%)	1273(56.1%)	0.96 (0.8 to 1)	0.7 (0.4 to 1.3)
	No	1031(44.9%)	1265(55.1%)		
Presence of co-morbid conditions	Yes	1012(44.5%)	1260(55.5%)	1 (0.9 to 1.1)	1 (0.6 to 1.9)
	No	1015(44.3%)	1278(55.7%)		
Vaccinated with at least one dose	Yes	108(57.8%)	79(42.6%)	1.8* (1.3 to 2.4) *	
	No	1919(43.8%)	2459(56.2%)		
Number of doses	0 dose (n=4378)	1919(43.8%)	2459(56.2%)		
	1 dose (n=135)	76(56.3%)	59(43.7%)	1.6*	
	2 doses (n=52)	32(61.5%)	20(38.5%)	2*	1.3 (0.6 to 2.4)
Type of vaccine	0 dose (n=4378)	1919(43.8%)	2459(56.2%)		
	Covishield (n=145)	81(55.9%)	64(44.1%)	1.6*	
	Covaxin (n=42)	27(64.3%)	15(35.7%)	2.3*	1.4 (0.7 to 2.9)

II. Breakthrough infection (n=45)

	Category	Yes (n=23)	No (n=22)	Odd's ratio (95%CI)	Adjusted OR (95%CI)
Sex	Female	10(58.8%)	7(41.2%)	1.6 (0.5 to 5.6)	1.6 (0.4 to 6)
	Male	13(46.4%)	15(53.6%)		
Age >56 years	Yes	9(42.9%)	12(57.1%)	0.5 (0.2 to 1.8)	0.33 (0.1 to 1.5)
	No	14(58.3%)	10(41.7%)		
Presence of co-morbid conditions	Yes	9(47.4%)	10(52.6%)	0.8 (0.2 to 2.5)	1.2 (0.3 to5.1)
	No	14(53.9%)	12(46.1%)		
Type of vaccine	Covaxin(n=15)	11(73.3%)	4(26.7%)	4.1* (1 to 16)	5.7* (1.3 to26)
	Covishield(n=30)	12(40%)	18(60%)		

*p value <0.05

Table 2: Effectiveness of Covid 19 vaccine against severe SARS CoV-2 infection

I. Baseline variables Vs Outcome (n=2027)

		Patients requiring ICU admission				Death			
Variables		**Yes (n=1050)**	**No (n=977)**	**Odd's ratio (95%CI)**	**Adjusted OR (95%CI)**	**Yes (n=511)**	**No (n=1516)**	**Odd's ratio (95%CI)**	**Adjusted OR (95%CI)**
Sex	Male	601 (55%)	491 (45%)	1.3 (1.1 to 1.6) *	2.9 (1 to 8.8) *	299 (27.4%)	793 (72.6%)	1.3 (1.1 to 1.6) *	3.3 (0.9 to 12.5)
	Female	449 (48%)	486 (52%)			212 (22.7%)	723 (77.3%)		
Age >56 years	Yes	611 (61.4%)	385 (38.6%)	2 (1.8 to 2.6) *	2.2 (0.8 to 6.4)	325 (32.6%)	671 (67.4%)	2.2 (1.8 to 2.7) *	1.3 (0.4 to 4.5)
	No	439 (42.6%)	592 (57.4%)			186 (18%)	845 (82%)		
Presence of co-morbid conditions	Yes	580 (57.3%)	432 (42.7%)	1.6(1.3 to 1.9) *	5.8 (1.8 to 18.6) *	358 (35.4%)	654 (64.6%)	3 (2.5 to 3.8) *	10.3 (2 to 52.6) *
	No	470 (46.3%)	545 (53.7%)			153 (15%)	862 (85%)		
II. Vaccination status Vs Outcome									
Vaccinated	Yes	26 (24%)	82(76%)	0.3 (0.2 to 0.4) *		17 (15.7%)	91 (84.3%)	0.5 (0.3 to 0.9) *	
	No	1024 (53.4%)	895 (46.6%)			494 (25.7%)	1425 (74.3%)		
Number of doses	0 dose (n=4378)	1024 (53.4%)	895 (46.6%)			494 (25.7%)	1425 (74.3%)		0.21 (0.04 to 1.1)
	1 dose (n=135)	23 (30.3%)	53 (69.7%)	0.4*	0.18 (0.04 to 0.8) *	15 (19.7%)	61 (80.3%)	0.7	
	2 doses (n=52)	3 (9.4%)	29 (90.6%)	0.09*		2(6.3%)	30 (93.7%)	0.19*	
Type of vaccine	No vaccination (n=4378)	1024 (53.4%)	895 (46.6%)			494 (25.7%)	1425 (74.3%)		1.3 (0.3 to 6.1)
	Covishield (n=145)	22 (27.2%)	59 (72.8%)	0.33*	0.85 (0.2 to 3.3)	14 (17.3%)	67 (82.7%)	0.6	
	Covaxin (n=42)	4(14.8%)	23 (85.2%)	0.15*		3(11.1%)	24(88.9%)	0.36*	

DISCUSSION

In our study, only 4% of SARI patients and 5.3 % of the RTPCR positive patients were vaccinated which is comparable to the district data as well as the state vaccine coverage during the initial phase. But it didn't reflect the current vaccine coverage. There is a possibility that vaccination could have reduced the need for hospitalization.

Our study couldn't find any protective effect of vaccination against new COVID 19 infections. Type of vaccine nor number of doses of vaccines has any effect on the occurrence of infection. 23 of them (51%) had a breakthrough infection. This is in contrast to the findings from other studies. Victor et al had documented that the protective effect of covid vaccination in preventing infection, hospitalization, need for oxygen and ICU admission were 65%, 77%, 92% and 94% respectively[10]. VIN-WIN cohort study conducted among 1.59 million health care workers and frontline workers of Indian Armed Forces showed a 93% reduction in breakthrough infection following Covishield vaccination[11]. Ella et al[4], Voysey et al[3], had also documented the protective effect of the vaccine in preventing infection. Pooled analysis of randomized control trials on ChAdOx1 nCoV-19 vaccines by Voysey et al showed that two standard doses had given 66.7% protection against hospitalization and symptomatic infections[12]. The efficacy of the covishield vaccine against symptomatic infections was found to be 76% after the first dose. If the interval between the first and second dose was extended to 12 weeks or more the efficacy rose to 91.6%[3]. But we couldn't find any protective effect of the vaccine in preventing the infection following vaccination.

Difference in health-seeking behaviour among the vaccinated and non-vaccinated patients, less number of vaccinated patients among the hospitalized patients and study design used in this study might be the factors[5].

In our study, it was well documented that vaccination offered significant protection against severe SARS Cov-2 infection. The protective effect shown by the vaccines in preventing a severe form of SARS Cov-2 infection among fully vaccinated patients was 82%. Fully vaccinated RTPCR positive patients had a statistically significant (82%) reduction (OR 0.09, AOR 0.18, 95% CI (0.04 to 0.8)) in the need for ICU admission and statistically non-significant reduction (AOR 0.21, 95% CI (0.04 to 1.1)) in the odds of dying. Covaxin vaccine seemed to be offering significantly higher protection against severe SARS Cov-2 infection as compared to the Covishield vaccine. However, after logistic regression analysis, both of them became not significant.

The protective effect shown by the vaccines in preventing a severe form of the disease found in our study is comparable with other studies except for mortality. Less number of patients with vaccination and fewer number deaths among the vaccinated people reported in our study could be the reason for this. Victor et al have reported a high protective effect of vaccination in preventing the need for oxygen (92%) and ICU admission (94%) among health care workers in India[10]. Jaiswal et al had documented 95 % effectiveness in preventing death among fully vaccinated people(High-risk group)[13]. Christie et al have documented that improved vaccination coverage has reduced hospital admissions, the need for oxygen supplementation and ICU admission in the United States of America[14]. Bernel et al have reported the real-world effectiveness of oxford Astra Zeneca in preventing ICU admissions as 73% in England[15]. Phase 3 trial results revealed that Covaxin had a protective effect of 93.4% against severe infections[16].The Vin-Win cohort study documented that the Covishield vaccine had shown 93% effectiveness against severe illness[11]. There is a paucity of studies in this field and more studies with bigger sample sizes are needed to conclude further.

Limitation:

The proportion of vaccinated and fully vaccinated patients, deaths among vaccinated people were low in our study so the results should be interpreted cautiously. Explicit research with more sample size and negative case-control study is quintessential to corroborate the findings.

CONCLUSION

Our study has found that vaccination didn't protect against new SARS Cov-2 infection. Covid vaccination significantly reduced the severity of illness among RT PCR positive patients. The protective effect shown by the vaccines in preventing a severe form of SARS Cov-2 infection among fully vaccinated patients was 82%.

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