



Pulmonary Medicine

A CROSS-SECTIONAL STUDY TO ESTIMATE THE IMPACT OF VACCINATION ON CLINICAL AND RADIOLOGICAL SEVERITY DURING THE THIRD WAVE OF COVID -19 PANDEMIC IN A TERTIARY COVID CARE HOSPITAL

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ABSTRACT **Background:** Real world studies have consistently shown high levels of short-term protection by vaccines against severe acute respiratory syndrome coronavirus-2.

Materials and methods: A cross sectional study was conducted in the outpatient department among patient who were tested positive for covid-19. The primary exposure of interest was vaccination with 2 doses of Covishield. The primary outcome was severity of disease measured in terms of incidence of hospitalisation, oxygenation and radiological findings. The time gap between last dose of vaccine and testing positive for the disease was also analysed to estimate the association. Patients with comorbid diseases were evaluated to assess the severity of infection in vaccinated and the unvaccinated.

Results: Among 80 patients who tested RTPCR positive for covid 19, it was found that 77.5% of the patients were fully vaccinated and 15.1 % were unvaccinated. Among the fully vaccinated, 24.19% were hospitalised whereas 91.6 % of unvaccinated patients required hospitalisation. 32 (40.3%) patients had other comorbid illnesses and among these 26 (81.2%) required hospitalisation. Waning of protection against hospitalisation was observed after 6.9 months.

Conclusion: The previous receipt of 2 doses of covid-19 vaccination was found to have significantly reduced the severity of disease and has favourable outcomes with less hospitalisation.

KEYWORDS : Covid 19, SARS-CoV-2 Vaccines, COVID-19 vaccine booster

Many efforts have been made to shed some light on COVID-19 vaccinations in the hopes of warding off the pandemic. Though safe and effective vaccines are pivotal in mitigation, it is not vaccine but vaccination that will probably end the pandemic. Real-world data have time and again shown high levels of short-term protection by vaccines against severe acute respiratory syndrome coronavirus-2 however being vaccinated still doesn't warrant a stroll without masks particularly because research is still ongoing into the duration of protection and the need for booster doses.

MATERIALS AND METHODS:

A cross sectional study was conducted during the third wave of covid 19 pandemic in the outpatient department of Government Medical College Kota among patient who were tested positive for covid-19. The primary exposure of interest was vaccination with 2 doses of covishield (ChAdOx1 nCoV-19 recombinant vaccine). The primary outcome was severity of disease measured in terms of oxygenation, incidence of hospitalisation and radiological findings^(1,2) in accordance with World Health Organization guideline. The time gap between last dose of vaccine and testing positive for the disease was also analysed to estimate the association. Patients with comorbid diseases were evaluated to assess the severity of infection in vaccinated and the unvaccinated.

RESULTS:

It was found that 85.1 % of the patients tested positive for covid 19 infection during the period of study were vaccinated with at least one dose of covishield, and 15.1 % were not vaccinated. Among the fully vaccinated (77.5%), only 24.19% were hospitalised with covid 19 infection whereas 91.6 % of unvaccinated patients required hospitalisation out of which 3 patients contracted disease during hospital stay during the third wave. 81.2% patients who required hospitalisation had significant comorbid illness making them immunocompromised. The demographics of the patients have been summarised in the table given below. (table 1)

Table 1: Demographics of patients:

CHARACTERISTICS	HOSPITALISED PATIENTS	HOME QUARANTINED
TOTAL NUMBER	32	48

MALE	23	32
FEMALE	9	16
MEAN AGE	59.29	38.75
FULLY VACCINATED	15 (46.8 %)	46 (95.8%)
SINGLE DOSE VACCINATED	6(18.7 %)	1(2.08%)
NOT VACCINATED	11 (34.3 %)	1(2.08%)
NO: OF IMMUNOCOMPROMISED	26 (81.2 %)	6(12.5%)

Among the patients managed on outpatient basis, the average time gap between last dose of vaccination and onset of illness is 4.06 months (± 2.26 , CI -95%) with an average SPO2 of 98.15% (± 0.90 , CI -95%) with all but two being fully vaccinated. The average age of this group being 38.4 with a male predominance.

The hospitalised patients had an average time gap of 6.90 months (± 4.48 , CI = 95%) with an average SPO2 of 87.03% (± 10.49 , CI -95%). A good proportion among hospitalised were vaccinated- 15 (46.8%) being fully vaccinated, 6 (18.7%) with one dose and 11 (34.3%) being unvaccinated. Among the fully vaccinated hospitalised patients, 13 had other co-morbid illnesses which accounts for about 86.5%. Pearson correlation coefficient was applied which showed positive correlation of baseline oxygen saturation with number of doses of vaccine ($r=0.243936$, $p<0.001$) and a negative correlation with timing of last dose ($r=-0.16774$, $p<0.001$)

Among hospitalised, 8 (25%) patients were asymptomatic and probably secondary cases who tested positive on pre-procedural/routine evaluations, 11 were managed in wards and 13 (40%) patients were admitted to an ICU. Among the patients in ICU, 7 (53.5%) were unvaccinated, 2 had incomplete vaccination status and 4 were fully vaccinated as per guidelines. No ethical issues were encountered during the study.

Table 2: clinical characteristics of vaccinated and unvaccinated patients:

CHARACTERISTICS	Unvaccinated (11)	Partially vaccinated (7)	Fully vaccinated (62)
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No: of hospitalised	11 (100%)	6 (85.7%)	15 (24.19 %)
Home quarantined	0	1 (2.08%)	47 (75.8%)
ICU admission	7 (63.63%)	2 (28.7%)	5 (8.06%)
Radiological evidence	72.7%	42.85%	24.5%
No: of immunocompromised	8 (72.72%)	5 (71.42%)	17(27.42%)

DISCUSSION:

In this study, vaccination with 2 doses of covishield was found to be associated with less severity of disease, lesser hospitalisation and favourable outcomes and my findings were consistent with previous studies conducted. Malhotra *et al*⁽⁵⁾ in their study concluded that COVID-19 vaccines have been reported to offer protection against variants, including Delta, after completion of the vaccination series, and the effect of partial uptake of vaccines has been found to be suboptimal to which our findings were in agreement.^(4,5)

Thiruvengadam Ramachandran *et al*⁽⁶⁾ in their study came to a conclusion that completion of 2 dose of vaccine offered better protection against moderate to severe disease with marginal death rate in comparison to single dose vaccination. In our study, we came to a similar conclusion with better protection among completely vaccinated in comparison to unvaccinated in terms of hospitalisations and ICU admissions but this could theoretically be confounded by comorbid illness and age. Our study showed that the presence of other co-morbid illness paved way to more hospitalisation, ICU admissions and more unfavourable outcomes irrespective of vaccination status. Observational data from Qatar indicated modestly reduced effectiveness against symptomatic disease caused by this variant but high levels of effectiveness against severe, critical or fatal disease in persons vaccinated⁽⁷⁾. Akin to this, no significant protection against symptomatic disease was found in our study with majority presenting with mild symptoms but fatality and criticality was significantly reduced.

As real-world data started approaching complete vaccination against covid, waning of immunity began to gain precedence among other concerns. Elderly and citizens with chronic illness were prioritised for immunisation the pattern of waning of immunity detected in multiple studies across the globe would have been confounded by age and co-existing conditions^(8,9). In this study, it was noticed that individuals who were vaccinated more than 6 months prior had severe illness clinically and radiologically with more ICU admissions. This pattern of waning of protection was observed in all age groups (table 3) hence validating the concern of requirement of booster dose.

Table 3: Age wise distribution of patients against weeks since receipt of last dose of vaccine:

	Not vaccinated	0- 5 wk	6-11 wk	12- 17wk	18-23 wk	>24 wk
Age < 18 yrs	1	0	0	1	1	0
19- 50 yrs	4	5	6	10	10	9
>50 yrs	6	3	7	3	3	9

LIMITATIONS:

There are several limitations to this study most important being the small sample size. The likelihood of false-positive and false negative molecular testing was not addressed in this study which is an important shortcoming considering the fact that the study was conducted only among the patients who tested positive in RTPCR. Many individuals will also have been previously infected, so the vaccine effectiveness measured is in the context of a population in which many might have already had natural exposure. The less severity of disease in general during the third wave can also be due to the less virulent variant rather than the protection offered by vaccine which is uncertain unless an antibody titre and genomic sequencing of virus is performed.

CONCLUSION:

In summary, the previous receipt of 2 doses of covid 19 vaccination has significantly reduced the severity of disease and had favourable outcomes with less hospitalisation. Comorbid illness have most likely outwitted the benefit from being fully vaccinated. From a public health perspective, it would be important to provide 2 doses of vaccine to all with priority given to individuals with comorbid illnesses. We identified greater waning in vaccine effectiveness against hospitalization after 6.9 months which warrants for studies to look for efficacy of booster doses along with antibody titres.

DECLARATION OF CONFLICT OF INTEREST: There are no

potential conflicts of interest with respect to research, authorship and publication of this research.

REFERENCES

- COVID-19 clinical management: living guidance. Geneva: World Health Organization, January 25, 2021 (<https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-1>).
- International guidelines for certification and classification (coding) of COVID-19 as cause of death. Geneva: World Health Organization, April 20, 2020 (https://www.who.int/classifications/icd/Guidelines_Cause_of_Death_COVID-19-20200420-EN.pdf?ua=1).
- SARS-CoV-2 Reinfection Rate and Estimated Effectiveness of the Inactivated Whole Virion Vaccine BBV152 Against Reinfection Among Health Care Workers in New Delhi, India. Sumit Malhotra, MD; Kalavani Mani, PhD; Rakesh Lodha, MD; Sameer Bakshi, MD; Vijay Prakash Mathur, MDS; Pooja Gupta, DM; Saurabh Kedia, DM; Jeeva Sankar, DM; Parmeshwar Kumar, MHA; Arvind Kumar, MD; Vineet Ahuja, DM; Subrata Sinha, PhD; Randeep Guleria, DM; and the COVID Reinfection AAIMS Consortium
- Amit S, Alessandra Beni S, Bibe A, et al. Post-vaccination COVID-19 among healthcare workers, Israel. Emerg Infect Dis 2021; 27:doi:10.3201/eid2704.210016
- Voysey M, Costa Clemens SA, Madhi SA, et al. Single dose administration, and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine. SSRN [Preprint]. February 1, 2021 [cited 2021 Feb 12]. https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3777268.
- Thiruvengadam, Ramachandran et al. "Effectiveness of ChAdOx1 nCoV-19 vaccine against SARS-CoV-2 infection during the delta (B.1.617.2) variant surge in India: a test-negative, case-control study and a mechanistic study of post-vaccination immune responses." The Lancet. Infectious diseases vol. 22,4 (2022): 473-482. doi:10.1016/S1473-3099(21)00680-0
- Lopez Bernal J, Andrews N, Gower C, et al. Effectiveness of Covid-19 vaccines against the B.1.617.2 (Delta) variant. N Engl J Med. 2021;385(7):585-594. doi:10.1056/NEJMoa2108891
- Abu-Raddad LJ, Chemaitelly H, Bertollini R. Waning mRNA-1273 vaccine effectiveness against SARS-CoV-2 infection in Qatar. N Engl J Med. DOI: 10.1056/NEJMc2119432
- Chemaitelly H, Tang P, Hasan MR, et al. Waning of BNT162b2 vaccine protection against SARS-CoV-2 infection in Qatar. N Engl J Med 2021;385(24):e83
- Baden LR, El Sahly HM, Essink B, et al: COVE Study Group. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. N Engl J Med 2021;384:403-16
- Voysey M, Clemens SAC, Madhi SA, et al; Oxford COVID Vaccine Trial Group. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. Lancet 2021;397:99-111
- Desai D, Khan AR, Soneja M et al. Effectiveness of an inactivated virus-based SARS-CoV-2 vaccine, BBV152, in India: a test-negative, case-control study. Lancet Infect Dis. 2021;S1473-3099(21)00674-5. doi:10.1016/S1473-3099(21)00674-5
- Andrews N, Tessier E, Stowe J, et al. Duration of protection against mild and severe disease by Covid-19 vaccines. N Engl J Med 2022;386:340-50
- Saeed GA, Gaba W, Shah A, et al. Correlation between Chest CT Severity Scores and the Clinical Parameters of Adult Patients with COVID-19 Pneumonia. Radiol Res Pract. 2021;2021:6697677. Published 2021 Jan 6. doi:10.1155/2021/6697677
- WHO evaluation of COVID-19 vaccine effectiveness 2021. <https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccine-effectiveness-measurement-2021.1>
- Dean NE, Hogan JW, Schnitzer ME. Covid-19 vaccine effectiveness and the test-negative design. N Engl J Med 2021; 385:1431-3.
- European Centre for Disease Prevention and Control. Reinfection with SARS CoV: considerations for public health response: ECDC:2020. Accessed August 31, 2021. <https://www.ecdc.europa.eu/sites/default/files/documents/Re-infection-and-viral-shedding-threat-assessment-brief.pdf>
- Ella R, Reddy S, Blackwelder W, et al Efficacy, safety, and lot to lot immunogenicity of an inactivated SARS CoV-2 vaccine (BBV152): a double-blind, randomized, controlled phase 3 trial. MedRxiv. Preprint posted online July 02, 2021. 2021;2021. 06.30. 21259439. doi:10.1101/2021.06.30.21259439
- Singh AK, Phatak SR, Singh R, et al. Antibody response after first and second-dose of ChAdOx1-nCoV (Covishield) and BBV-152 (Covaxin) among health care workers in India: the final results of cross-sectional coronavirus vaccine-induced antibody titre (COVAT) study. Vaccine. 2021;39(44):6492-6509. doi:10.1016/j.vaccine.2021.09.055
- Kant R, Dwivedi G, Zaman K, et al. Immunogenicity and safety of a heterologous prime-boost COVID-19 vaccine schedule: ChAdOx1 vaccine Covishield followed by BBV152 Covaxin. J Travel Med. 2021;taab166. doi:10.1093/jtm/taab166
- Hunter PR, Brainard J. Estimating the effectiveness of the Pfizer COVID-19 BNT162b2 vaccine after a single dose: a reanalysis of a study of 'real-world' vaccination outcomes from Israel. February 3, 2021 (<https://www.medrxiv.org/content/10.1101/2021.02.01.21250957v1>). preprint.
- Hall VJ, Foulkes S, Saei A, et al. COVID-19 vaccine coverage in health-care workers in England and effectiveness of BNT162b2 mRNA vaccine against infection (SIREN): a prospective, multicentre, cohort study. Lancet 2021;397:1725-35.