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RESEARCH ARTICLE OPEN ACCESS

SARS-CoV-2 Non Responders - An Analysis of Non Responsiveness to SARS-CoV-2 Vaccines among Healthcare Workers in 2021

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Abstract

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS CoV-2) possess high mortality and morbidity across the globe. In India, BBV-152 (Covaxin™) and ChAdOx1-nCOV (Covishield™) vaccines are now being used to limit the spread of SARS-CoV-2 Infection. A Cross sectional observational study was designed to analyze the Antibody immune response to SARS CoV-2 vaccine quantitatively among Health Care Workers and it was correlated with age, sex, other comorbidities and blood group. A total of 160 fully vaccinated HCWs, the Anti-SARS-CoV-2 level was estimated by using Chemiluminescence Immuno Assay. A protective immune response following the complete course of the SARS-CoV-2 vaccine should be ≥ 1.00 S/C. A total of 160 HCWs (82 Male, 78 Female) who had completed both the doses of Covishield (n=128) and Covaxin (n=32). Both the vaccine recipient had mild to moderate symptoms and none of the HCWs had severe adverse events after administration of vaccine. Out of which, 143 (89.3%) HCWs showed seropositive and 17 (10.7%) HCWs showed seronegative. There was no notable variation in sex and other co-morbidities. Significantly, reduced antibody titers towards SARS-CoV-2 vaccine was noted among individuals aged ≤ 60 years and O+ve Blood group. Both the vaccines obtained successful immune response after their complete course, even though there was a significantly higher seropositivity rate in Covishield in spite of Covaxin recipients. Further, genomic correlative advanced studies can conclude the significance of non-responsiveness to SARS-CoV-2 vaccines among the HCWs.

Keywords: SARS-CoV-2 infection, SARS-CoV-2 Vaccines, Health Care Workers, Antibody immune response to SARS-CoV-2, Non Responsiveness

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Abbreviation: Anti- SARS CoV-2 - Antibody immune response to Severe Acute Respiratory Syndrome Corona Virus 2. ASC - Antibody Secreting Cells, BBV-152 - Whole-Virion Inactivated SARS-CoV-2 Vaccine, BNT162b2 mRNA - BioNTech 162 b 2 Messenger Ribonucleic Acid, ChAdOx1-nCOV-19 - Chimpanzee (Ch) Adenovirus-vectored vaccine (Ad), developed by the University of Oxford (Ox) to induce an immune response to novel coronavirus (nCoV-19), CLIA - Chemiluminescence Immuno Assay, SARS CoV 2 - Severe Acute Respiratory Syndrome Corona Virus 2.

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INTRODUCTION

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has impacted 328 million population including 5.5 million deceased across the globe as per the World Health Organization (WHO) till 18th January 2022.[1] On 02nd November 2020, European Medicine Agency in the United Kingdom approved 1st mRNA vaccine - BNT162b2 mRNA (Pfizer–BioNTech vaccine).[2] In India, BBV-152 (Covaxin™) and ChAdOx1-nCOV (Covishield™) are the two vaccines approved by Emergency Use Authorization started from 16th January 2021.[3] In Oxford University and AstraZeneca, ChAdOx1-nCOV is produced from the genetically modified human embryonic kidney 293 cells by recombinant replication-deficient chimpanzee adenovirus-vectored vaccine which encodes spike antigen of SARS-CoV-2 spike.[4] BBV-152 is an ß-propiolactone whole virion vaccine that is inactivated and contains SARS-CoV-2 proteins adjuvant together with imidazoquinolinone, a Toll-like receptor 7/8 manufactured in co-operation with Indian Council of Medical Research by Bharat Biotech, Hyderabad.[5]

Notably, humoral immune response to vaccination or acquired infection leads to immunological modification in humans. Antibody secreting cells (ASC) produces antibodies that provide protective immunity and due to production of long-lived memory B cells, they turn effective in increasing recall responses when exposed again. When protective immunity has failed due to circulating antibodies, the memory B cells lead the recall response over generating newer antibodies by in case of re-initiating germinal center reaction to produce new antibodies or formation of new ASC. These immunological memories (Memory B Cells and Antibodies) are enduring for nearly 6 months as suggested by the experts.[6]

After the phase three Clinical Trials, it was recommended that the BBV-152 and ChAdOx1-nCOV vaccines are safe and effective.[7] The recipient of the vaccines were - Healthcare workers (HCWs), Frontline workers and people > 45 years' age group. In India, from 1st May 2021, vaccination was provided to all adults aged >18 years.[8] As per World Health Organization (14th January 2022), 939 Crore vaccine doses have been administered. 392 Crore population were fully vaccinated globally.[1] In India, at present (16th January 2022) about 157 crore population are vaccinated out of which 65.6 Crore people are fully vaccinated against SARS-CoV-2.[9] A protective immune response following the complete course of the SARS-CoV-2 vaccine should be ≥ 1.00 S/C (reactive or seropositive) whereas < 1 S/C (non-reactive or seronegative).

There is a limited data available on how much and how long these novel vaccines can induce an immunogenicity among HCWs, both at the cellular and humoral levels. Hence, we perform this cross-sectional observational study to assess the Antibody immune response to SARS-CoV-2 vaccine quantitatively among HCWs and it was correlated with age, sex, other comorbidities and blood grouping at a tertiary care setting.

MATERIALS AND METHOD

A Cross-Sectional observational study was carried out at a tertiary care SARS-CoV-2 exclusive Centre in Tamilnadu, South India. A total of 160 fully vaccinated HCWs were tested for Anti SARS-CoV-2. Ethical approval (2923/IEC/2021) was obtained from Institutional Ethical Committee. Participants who had completed their course of SARS-CoV-2 vaccine, aged between 18 to 65 were included and those who did not get completely vaccinated, aged <18 and > 65 years and HCWs who were recently administered the 2nd dose of SARS-CoV-2 vaccine were excluded from the study. A patient information sheet along with an informed consent form was procured and correspondingly approved by the HCWs. An authenticated questionnaire was distributed to all HCWs who participated in the study and were duly filled. Under aseptic precautions, a whole blood sample was collected by experienced phlebotomist as per World Health Organization guidelines,[10] and centrifuged after clot formation. Quantitative detection of SARS-CoV-2 Antibody was performed using Chemiluminescence Immuno Assay (CLIA) method as per manufacturer protocol (Ortho Diagnostics Pvt. Ltd.). A protective immune reaction following the complete course of the SARS-CoV-2 vaccine should be ≥ 1.00 S/C (reactive or seropositive) versus < 1 S/C (non-reactive or seronegative) as per manufacturer interpretation (Ortho Diagnostics Pvt. Ltd.).

Table 1. Socio-Demographic And Comorbidities Analysis On Seropositivity And Seronegativity Rate Among Health Care Workers

Characteristics	Overall (n=160)	Seropositivity rate (n=143)	Seronegativity rate (n=17)
		Age (in Years)	
≤ 60, n (%)	134 (83.7%)	123 (86%)	11 (64.7%)
61-65, n (%)	26 (16.3%)	20 (14%)	6 (35.3%)
		Sex	
Male, n (%)	82 (51.2%)	73 (51%)	9 (52.9%)
Female, n (%)	78(48.8%)	70 (49%)	8 (47.1%)
		Blood group	
O+ve n (%)	59 (36.8%)	52 (36.4%)	7 (41.2%)
O-ve n (%)	2 (1.3%)	1 (0.7%)	1 (5.9%)
A+ve n (%)	26 (16.2%)	23 (16.1%)	3 (17.6%)
A –ve n (%)	3 (1.8%)	3 (2%)	0 (0%)
AB +ve n (%)	7 (4.4%)	6 (4.2%)	1 (5.9%)
AB –ve n (%)	10 (6.3%)	9 (6.3%)	1 (5.9%)
B+ve n (%)	51 (31.9%)	47 (32.9%)	4 (23.5%)
B-ve n (%)	2 (1.3%)	2 (1.4%)	0 (0%)
		Comorbidities	
Diabetes mellitus n (%)	19 (11.8%)	17 (11.9%)	2 (11.8%)
Hypertension n (%)	17 (10.6%)	15 (10.5%)	2 (11.8%)
Pulmonary Disease n (%)	3 (1.8%)	2 (1.4%)	1 (5.9%)
Cardiac Disorder n (%)	3 (1.8%)	3 (2%)	0 (0%)
No Comorbidities n(%)	118 (74%)	106 (74.2%)	12 (70.5%)
		Types of Vaccine	
Covishield, n (%)	128 (80%)	122 (85.3%)	6 (35.2%)
Covaxin, n (%)	32 (20%)	21 (14.7%)	11 (64.8%)

RESULTS

A total of 160 fully vaccinated HCWs was analyzed for Anti- SARS-CoV-2, in which the males were more in count of 82 (51.2%), than the females of 78 (48.8%). Among them, 134 (83.7%) were aged ≤ 60 years and 26 (16.3%) were aged between 61 to 65 years. Out of 160 HCWs, based on blood groups - A+ve, A-ve, O+ve, O-ve, AB+ve, AB-ve, B+ve and B-ve were 59 (36.8%), 2 (1.3%), 26 (16.2%), 3 (1.8%), 7 (4.4%), 10 (6.3%), 51 (31.9%) and 2 (1.3%) respectively. Among the 160 HCWs, 33 (20.6%) had exposure to SARS-CoV-2 Infection and 42 (26.2%) had comorbidities before vaccination, out of 42 HCWs - 19 (45.3%) had Diabetes Mellitus, 17 (40.5%) had Hypertension, 3 (7.1%) had pulmonary diseases and 3 (7.1%) had a cardiac disorder as shown in Table 1.

A sum of 160 HCWs, 128 (80%) and 32 (20%) had received Covishield and Covaxin respectively (Table 1). Out of which 99 (61.8%) HCWs had no symptoms whereas 61 (38.2%) HCWs had mild to moderate symptoms like fever, myalgia, persistent abdominal pain, headache, fainting spells, chest pain, excessive sweat and diarrhea which occurred within 12-24 hours of administration of vaccines. Out of 160 HCWs, 143 (89.3%) and 17 (10.7%) HCWs had seropositivity and seronegativity respectively. In particular, there was a significantly higher seropositivity rate in Covishield vs. Covaxin recipients; 122 (95.3%) vs. 21 (65.6%) as shown in Table 1.

Out of 17 (10.7%) Seronegative HCWs, the number of males and females were 9 (52.9%) and 8 (47.1%) respectively, followed by age, ≤ 60 years and between 61 to 65 were 11 (64.7%) and 6 (35.3%) respectively. Seronegative ratio in blood group were as follows: 7 (41.2%) of O+ve, 1 (5.9%) of O-ve, 3 (17.6%) of A+ve, 1 (5.9%) of AB+ve, 1 (5.9%) of AB-ve and 4 (23.5%) of B+ve. Seronegative rate of comorbidities among HCWs shows 2 (11.8%) of Diabetes mellitus, 2 (11.8%) of Hypertension, 1 (5.9%) of pulmonary disease and 12 (70.5%) had no comorbidities. Out of 17 (10.7%) Seronegative HCWs, 6 (35.2%) were administered

with Covishield and 11 (64.8%) were administered with Covaxin vaccines (Table 1).

Out of the 160 vaccine recipients, 19 (11.8%) developed SARS-CoV-2 infection after their second dose of vaccination. This is known as breakthrough infections (defined as infection of SARS-CoV-2 following the second dose in > 2 weeks) Breakthrough infections among Covishield recipients were 16 (84.2%) and 3 (15.8%) in Covaxin recipients with mild to moderate range and cured without hospitalization. There was no mortality among them.

DISCUSSION

Antibody response contributes substantially to establish a protective immune response over SARS-CoV-2 infection. Despite different titre values of antibody failing to involve in the immediate protection from SARS-CoV-2 infection, it could be employed as a surrogate biomarker of antibody response in evaluating humoral immunity against SARS-CoV-2 infection.[18] This present cross-sectional study indicated an overall induced seropositivity rate of Anti SARS-CoV-2 in 143 (89.3%) HCWs after two complete doses of both the SARS-CoV-2 vaccines (Covishield 95.3% and Covaxin 65.6% respectively). Previous studies suggest that the two-dose of SARS-CoV-2 vaccines induced more neutralizing antibodies with a past history of natural infection and recovery from SARS-CoV-2 infection.[11] Notably, both SARS-CoV-2 vaccines demonstrated an increased seropositivity rate after completion of the second dose. Ghosh et.al conducted a study and reported that the overall seropositivity rate of Anti SARS-CoV-2 among HCWs were 91.8 – 94.9%.[12] Similarly, Benal JL et.al and Ward H et.al reported the seropositivity rate of 89% and 91.1% respectively.[13,14] The Seronegativity rate of Anti SARS-CoV-2 in this present study were reported 10.7% which was lesser than the previous study results were found to be 18.6% and 13.3%.[13,15] However, the seropositivity rate was lower in Covaxin than Covishield recipients (65.6% vs. 95.3% respectively) and our study results were in accordance with the study findings of Singh AK et al.[3]

There was no notable variation in seropositive rate with respect to sex, age, blood group and other co-morbidities along with its duration and treatment. Significantly, there was a low seropositivity rate of Anti-SARS-CoV-2 observed among those aged ≤ 60 years and the O^+ Blood group. Particularly, there was no considerable difference in both the vaccines showing seropositive rate among SARS-CoV-2 recovered and SARS-CoV-2 naïve participants. Therefore, our results are in concordance with the study findings of Awadhesh Kumar Singh et al. and Ella et al.[3,15] Several other studies also demonstrated that there was no significant relation to antibody responses with comorbidities following vaccination.[17] Therefore, further studies would have to be conducted in order to prove the correlation or lack between the comorbidities in a wider population for future scope.

Real-time analysis of breakthrough infections was done after completing a full vaccination course.[16] Out of 19 HCWs, 16 (84.2%) Covishield recipients and 3 (15.8%) Covaxin recipients had acquired breakthrough infections with mild to moderate SARS-CoV-2 infections with a 100% recovery rate. In this present study, the median days among the 2nd dose and positive SARS-CoV2 infection were nearly 30 days which is too long compared to earlier study results which showed 5 days and 47 days.[13,14] Both vaccines elicited good immune responses after completion of 2 doses.[3]

CONCLUSION

This cross-sectional observational study indicates that both SARS-CoV-2 vaccines have induced immune response towards anti-spike antigen in 89.3% of SARS-CoV-2 retrieved and naïve individuals following the completion of two doses. On analyzing the data of our study and comparing it with the clinical correlation, the predominance of seronegative rate amidst HCWs mostly belonged to the age group of ≤ 60 years and O+ve Blood group. Notably, Covishield recipients had a seropositivity rate higher than Covaxin recipients. Irrespective of other co-morbidities, it was identified that the vaccine recipients acquired a strong immune response against the infection. Thus, all HCWs are highly recommended to get the booster dose to increase their immunogenicity. Further, genomic correlative advanced studies can conclude the significance of SARS-CoV-2 seronegative rate among the HCWs.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTION

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

FUNDING

None.

DATA AVAILABILITY

All datasets generated or analyzed during this study are included in the manuscript.

ETHICS STATEMENT

This study was approved by the Institutional Ethics Committee, SRM Medical College Hospital and Research Centre, India with reference number 2923/IEC/2021.

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