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Humoral Immunogenicity of the Covid-19 Vaccine (Covisheild- Chadox1) At the End of 4th Week of Second Dose

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Abstract

BACKGROUND

Assessment of the humoral immunogenicity of vaccines against the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in local populations is essential. Anti SARS nCoV II spike protein (RBD) antibodies are known to entrap the unbound SARS nCov II viruses and prevent entry and further progress of viral replication. Covishelid vaccine was the first vaccine candidate to receive Emergency use authorization in India for nation wide vaccination of health care workers. The estimation of neutralizing antibodies was done on completion of 4 week after the second dose of Covishield vaccine.

METHODS

164 health care workers including hospital nursing staff, lab technicians and doctors who have had received both the doses of vaccine and completed 4 weeks, were enrolled in the study. Estimation of Anti SARS nCoV spike protein (RBD) antibodies was done using CLIA based kit by Beckman-Coulter.

RESULTS

The participants included 105 males (64%) and 59 Females (36%). The estimation of neutralizing IgG antibodies against RBD of SARS nCoV 2 was done at 4 weeks of receipt of second dose. Overall observed sero-conversion rate was in 149 (90.85%) while 15 (9.15%) had no detectable antibodies. Age wise sero - conversion showed: age group <35 years (95.71%), age group 35-55 years 90.27% and in age group >55 years 77.28%. Diabetes was one of the co-morbidities showed less seroconversion rate. Two candidates were with sickle cell disease, both showed seroconversion.

CONCLUSIONS

Overall humoral mmunogenicity of Covisheild vaccine was > 90 % . The vaccine response was observed better in agegroup < 35 while age group > 55 years had more vaccine non-responders. Individuals with DM were observed to have lower vaccine response. The protective antibody was detected in 90.1 % population. Larger cohort study is required to evaluate effect of comorbidy on seroconcersion rate. As there were individuals with seroconversion showing very low antibody titres it is suggested that for better protection against SARS nCoV 2 and the variants one needs to evaluate longevity of humoral immune response.

Key words: Covid19, Receptor binding domain (RBD)of spike proteins, Recombinant, Covisheild

Introduction

Coronavirus disease 2019 (COVID-19), a disease caused by the novel coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged in China and rapidly spread across the world.[1] The World Health Organization declared COVID-19 as a pandemic on 11 March 2020, and by

09 December 2020, there have been 67,780,361 confirmed cases worldwide, including 1,551,214 deaths. Daily new cases continue to emerge worldwide, with second spikes/waves in some areas.

Corona virus that belongs to the beta-corona virus genus and is closely related to other corona viruses, namely SARS-CoV (79% genetic similarity) and Middle East respiratory syndrome corona virus (MERS-CoV). [2, 3] The main mode of transmission of SARS-CoV-2 is via respiratory droplets.

The incubation period of SARS-CoV-2 ranges between 2 and 14 days 4,5 with a median of 4–5 days; 6–9 however, most (97.5%) infected patients develop symptoms within 11.5 days. 8 Infected individuals can present with no symptoms, but most develop mild/moderate disease, while others succumb to severe/critical disease. [4, 5]

Despite many intense on-going trials, development of curative targeted therapy for this devastating pandemic disease looked a distant possibility. Hence, the world urgently needed safe and effective vaccine strategies for the prevention of new infections from this virus.

Analysis of the nucleic acid sequence within the spike protein receptor-binding domain (RBD) suggests that SAR-CoV-2 uses angiotensin-converting enzyme 2 (ACE2) as a cell receptor for cellular entry and infection, [4, 6, 7]

A good vaccine candidate against viral infections would be expected to induce a type of protective immune response similar to that elicited by natural infection. Therefore, a better understanding of both protective and pathogenic immune responses elicited by SARS-CoV-2 is essential.

This knowledge can aid in the design of vaccines that are most likely to elicit protective immunity. Current understanding of immune responses during Covid-19, although very limited, can help in the selection of strategies most likely to elicit protective immunity against SARS-CoV-2.If natural infection elicits potent T-cell responses, which are commonly associated with protective antiviral immunity, then this would aid in rapid vaccine development.[8] These studies high light the importance of elucidating the nature of protective versus pathogenic T-cell responses which is important for the design of vaccines that are both effective and safe.[9] T-cell responses are critical in eliminating the virus and should be considered in vaccine strategies. However, whether T-cell responses alone are capable of preventing infection in human settings remains to be investigated.[10]

Currently, there are three candidate vaccines with excellent efficacy and little side effects, these include: BioNTech / Fosun Pharma /Pfizer, Moderna /NIAID, and University of Oxford/AstraZeneca. Serum Institute of India's Covid 19 vaccine called Covishield is a version of Oxford AstraZeneca vaccine that is manufactured in India. ChAdOx1 nCoV-19 (Covishield) is a candidate SARS-CoV-2 vaccine comprising a replication-deficient simian adenovirus expressing full-length SARS-CoV-2 spike protein given as either a one- or two-dose regimen.[11] Preliminary safety and immunogenicity data from a phase 1/2 trial of the ChAdOx1 nCoV-19 vaccine (NCT04400838) demonstrated that promising results The vaccine was tolerated, with successful induction of neutralizing antibodies and antigen-specific T cells against the SARS-CoV-2 spike protein. These data supported progression to phase 3 trials with a two-dose regimen, and we have now expanded our immunogenicity analysis to explore a wider range of the immunological phenotypes induced.

Different vaccines have been developed so far for the prophylactic use against COVID-19. Many vaccine candidates are under phase trials for use against COVID-19. Some of these have been given emergency use authorization by the international and national authorities. Basically four types of vaccines are currently available mRNA vaccine, Viral Vector vaccine, inactivated viral vaccine and Sub unit vaccine. All the vaccines basically target the SARS-CoV-2 spike proteins as the antibodies against these are proved in vitro as virus neutralizing antibodies.

Currently, there are no defined correlates of protection against COVID-19 infection, and the immunological thresholds required for vaccine efficacy remain undefined.[6] Clinical studies have suggested a protective role for both humoral and cell-mediated immunity in recovery from SARS-CoV-2 infection.[12]

Covishield vaccine is ChAdOx1 nCoV- 19 Corona Virus Vaccine (Recombinant) vaccine. Mechanism of action COVISHIELD™ is a monovalent vaccine composed of a single recombinant, replication-

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deficient chimpanzee adenovirus (ChAdOx1) vector encoding the S glycoprotein of SARS-CoV-2. Following administration, the S glycoprotein of SARS-CoV-2 is expressed locally stimulating neutralizing antibody and cellular immune responses.[11]

Since anti SARS-CoV-2 Receptor Binding Domin (RBD) antibodies are neutralizing antibodies as they trap the viruses and prevent their entry into the cells and further replication. We propose to study the qualitative analysis of such antibody titres formed as a result of vaccination (Covishield) upon completion of four weeks of second dose.

The Aims of the Study

1. To study the immunogenicity of covishield vaccine by estimation of anti SARS covid 19 spike protein antibodies.
2. Comparison of antibody titres in relation to the age groups below 35 years, 35-55 years and 55 years and above.
3. Antibody titres in relation to the associated co-morbidity

We propose to estimate overall immunogenicity of Covisheild vaccine after 4 weeks of receiving two recommended doses of vaccine.

Material Method

Blood samples of 164 health care workers, recipients of Covishield vaccine, at the end of forth week of second shot of the vaccine. The anti SARS nCoV 2 spike proteins Ig G antibody estimation was done by chemiluminescent immunoassay using kit from Beckman Coulter SARS-CoV-2 IgG assay.

Inclusion Criteria:

All the recipiants of Covishield vaccine of phase one vaccination schedule. (All the health care workers.)

Exclusion criteria: As per the conditions of phase one vaccination schedule

1. Preganant women
2. Lactating mothers.
3. Individuals with known immunodeficiency

Result

Estimation of anti SARS nCov 2 RBD IgG antibodies was done using chemiluminescent immunoassay using kit from Beckman Coulter SARS-CoV-2 IgG assay. The Beckman Coulter SARS-CoV-2 IgG assay kit is a semi-quantitative method and detects only anti SARS-Cov-2 RBD IgG antibodies. The antibody levels are reported as S/CO. The sensitivity of the test is 100% after 18 days and the specificity is 99.6%. The tests were performed strictly as per the protocol recommended by the manufacturer.

The study comprised of 164 participants. The male : female ratio was 105:59. The cohort age range was 18 to 62 years.

Table no. 1 Humoral Immune response in Males & in Females:

Gender	Responders	Non Responders	Total
Male	95 (90.47%)	10 (9.52%)	105
Female	54 (91.52%)	5 (8.48%)	59

Vaccine responders were with detectable antibody titres was 90.85% and 9.15% individuals did not have detectable antibodies.

Table 2: Influence of age on humoral Immune response:

Age	Gender	Responders	Non Responders	Total
<35	M	39 (95.12%)	2 (4.87%)	41
	F	28 (96.55%)	1 (3.44%)	29
35-55	M	42 (91.30%)	4 (8.70%)	46
	F	23 (88.46%)	3 (11.54)	26
55<	M	14 (77.78%)	4 (22.22%)	18
	F	3(75%)	1 (25%)	4

Chart no 1: Post-vaccination age wise antibody levels:

The highest antibody levels detected 48.09 S/Co.

The antibody response and associated co-morbidities is shown in table no 3.

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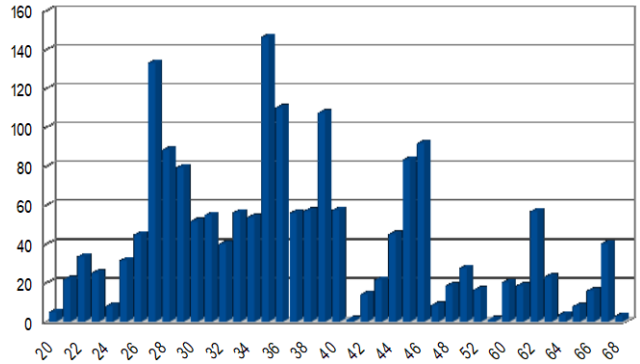

Table 3: Effect of co-morbidity on humoral immune response

Comorbidity	Responders	Non Responders	Total
Sickel cell Diseases	2 (100%)	0	2
Hypertension	1 (100%)	0	1
DM	3 (60%)	2 (40%)	5
DM, metformin	1 (100%)	0	1
Metformine	1 (100%)	0	1
Thyroid	1 (100%)	0	1
Aspirin	2(66.7%)	1 (33.3%)	3
Total	11 (78.5%)	3 (21.5%)	14

Discussion

The present study was conducted to ascertain the humoral immune response to the Covisheild vaccine after 4 weeks of second dose administration. The antibody measurement was performed after 4 weeks of second vaccine dose to ascertain the seroconversion . Overall humoral immunogenicity was about 90 % . The number of non responders in males was higher than in females.

We also tried to evaluate age wise humoral immune response to Covisheild vaccine and the study indicates the seroconversion rate was better amongst individuals with age less than 55 and as the age increases the seroconversion rate goes down.

Although there is no established understanding between the level of antibodies and protection especially to high risk group individuals we tried to see the levels of antibody titres in different age groups and found that high levels of protective antibodies were observed in individuals with age less than 40 years.

The second wave in India was due the delta variant of SARS nCoV 2 and the breakthrough infections were observed in vaccinated individuals. We at our Institute observed that incidence of severe infections or hospitalization was observed in very low percentage of vaccinated individuals. (still unpublished data.) In a nation wide surveillance conducted by ICMR reported majority of breakthrough infection were caused by delta variant of only 9.8 % required hospitalization and the observed mortality was 0.4 %. (data available on ICMR site.) The role of neutralizing antibodies or T cell immunity in protection against delta variant needs to be studied. Aslo the actual titres of antibodies required for protection against Delta variant is a matter of interest.

Larger cohort studies are required to analyze the effect of co-morbidity on the humoral immune response as the number of individuals with co-morbidity was very sketchy in the present study.

There were 2 individuals with sickle cell disease and both showed seroconversion.

Conclusion

The protective antibody was detected in 90.1 % population. Larger cohort study is required to evaluate effect of comorbidy on seroconcersion rate. As there were individuals with seroconversion showing very low antibody titres it is suggested that for better protection against SARS nCoV 2 and the variants one needs to evaluate longevity of humoral immune response.

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