STUDYING THE EFFICACY, SAFETY, AND IMMUNOGENICITY OF THE COVISHIELD VACCINE IN HEALTHCARE PERSONNEL IN AN INDIAN SCENARIO

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ABSTRACT

Background: COVID-19 has largely affected humans with high infection spread and mortality rates globally including India with no specific vaccine or therapy proven effective for its management as the immune response to COVID-19 is not well understood. Covishield has been largely distributed and administered in Indian subjects. However, its efficacy and safety are still unclear raising doubts.

Aim: The present study aimed to assess the efficacy, safety, and immunogenicity of the Covishield vaccine in healthcare personnel in India.

Methods: In 244 healthcare workers, SARS CoV2 IgG antibodies were assessed before and following the vaccination with two doses of Covishield given at 4 to 6 weeks apart. The efficacy of the vaccine and adverse effects after immunization were evaluated till two months after vaccination. The most common side-effect seen after the 1st dose was pain at the site of injection reported in 53.27% (n=130) study subjects followed by fever in 27.86% (n=68) study subjects, body ache in 22.95% (n=56) study subjects

Results: Before vaccination, IgG was positive in 21.31% (n=52) study subjects and was negative in 78.68% (n=192) study subjects. Post-vaccination, IgG-positive status was seen in 69.67% (n=170) study subjects and was not seen in 30.32% (n=74) study subjects. In the infected group having 62 subjects, post-vaccination IgG positive was seen in 96.77% (n=60) study subjects and not seen in 3.22% (n=2) study subjects. In the uninfected group including the 182 subjects, post-

vaccination IgG positive was seen in 60.43% (n=110) study subjects and was not seen in 39.56% (n=72) study subjects respectively. After 2nd dose, the most common side-effect was pain at the site of injection seen in 24.59% (n=60) study subjects followed by headache in 12.29% (n=30) study subjects, fever in 7.37% (n=18) study subjects, body ache in 3.27% (n=8) participants, low backache and fatigue in 1.63% (n=4) study subjects each and local swelling in 0.81% (n=2) study subjects respectively. All the side effects had a non-significant difference except body ache which was significantly higher after 1st dose with p=0.02.

Conclusion: Covishield vaccine has acceptable safety profile levels with increased seropositivity with more intervals in the two doses of the Covishield vaccine. Covishield does not prevent breakthrough infection. However, it can reduce the infection severity of COVID-19.

Keywords: COVID-19, Covishield, Immunization, seropositivity, vaccination

INTRODUCTION

SAS-CoV-2 (severe acute respiratory syndrome) was first reported in 2019 in Wuhan, China which later spread globally and was declared a pandemic by WHO (World Health Organization) in 2020. COVID-19 has affected nearly 186 million subjects globally with a high mortality rate of 4.01 million reported deaths by July 2021.[1] Although all the subjects from all age ranges are at risk of encountering COVID-19 infection, a higher risk has been reported in healthcare personnel with increased transmission risks to a family member and patients in contact, patient care disruption, mental stress, morbidity, and mortality rates. Hence, it has been globally considered to detect, isolate, and treat healthcare professionals with COVID-19 globally.[2,3]

With the COVID-19 being a newer identified disease entity in humans, no specific vaccine or therapeutic agent has been considered for COVID-19. This can also be attributed to the poor and unclear understanding of the protective immune response in the COVID-19 disease. With the introduction of different vaccines for the prevention of COVID-19, it is yet not clear which vaccine will prove to be the most efficacious and successful.[4] Hence, it is vital to develop different vaccine strategies and platforms side by side. However, with the high mortality rates and widespread infection, an urgent need was warranted for vaccine development which led to a proposed paradigm with shortened vaccine development timeline from 10-15 years to 1-2 years.[5]

Globally, 160 vaccine types have been identified and only a few have entered phases I, II, and III of the clinical trials. One such vaccine is Covishield manufactured by the Serum Institute of India, Pune which is a recombinant Chimpanzee Adenovirus vector vaccine that codes the SARS-Cov-2 spike S glycoprotein.[6] The technology for Covishield is taken from Oxford University/AstraZeneca. Considering the permission of its use, it was advised to be used in emergency conditions with the restriction. The present study aimed to assess the efficacy, safety, and immunogenicity of the Covishield vaccine in healthcare personnel in India.[7]

The assessment was done to assess the antibody response after complete vaccination with the two doses of Covishield. Also, the antibody response was compared in uninfected and infected healthcare professionals. Prevaccination and Postvaccination antibody response was compared in the infected subjects.[8] The overall safety profile of the Covishield was assessed after vaccination.

Postvaccination antibody response was compared in an interval of 4 to 6 weeks between two vaccination doses in the uninfected subjects.

MATERIALS AND METHODS

The present prospective analytical study aimed to assess the efficacy, safety, and immunogenicity of the Covishield vaccine in healthcare personnel in India. The study was done at Department of General Medicine, SMBT IMSRC College Dhamangaon Igatpuri, Nashik, Maharashtra after the clearance was given by the Concerned Institutional Ethical committee. The study population was comprised of the health care personnel of the Institute. After explaining the detailed study design, informed consent was taken from all the participants in both written and verbal format.

The study included 244 subjects from both genders that were healthcare personnel irrespective of their cadre, The inclusion criteria were healthcare personnel, of age more than 18 years, and both COVID uninfected and infected study subjects. Before the vaccination, screening for SARS-CoV-2 IgG antibodies was done for all the study participants. The infected group was comprised of the subjects who were positive for the pre-vaccination antibodies and had a previous history of infection with the COVID comprising the 62 subjects. The subjects with no history of previous COVID infection and no pre-screening antibodies were considered uninfected group subjects comprising 182 study participants. Another subgroup was comprised of subjects where the 2^{nd} dose was delayed for 2 weeks irrespective of any reason. Hence, the study comprised two groups who took the second dose at 4 weeks and 6 weeks intervals.

Concerning the administration of Covishield in the study subjects, 0.5ml vaccine was given via intramuscular route in the deltoid region at 4 weeks intervals and in the subject after 6 weeks, a second dose of the vaccine was given.

For assessing the antibodies, 2ml of the venous blood was collected using the sterile and aseptic method at two-time intervals which is just before the vaccination and 28 days following the second vaccine dose. SARS Cov-2 IgG antibodies were evaluated using a micro-ELISA kit to quantitively detect the IgG antibodies for SARS CoV-2. Whole-cell antigen coated on a microtiter plate was used as SARS CoV2 antigen in both groups.

The results were interpreted following the instructions by the manufacturers. Samples with cut-off and positive to negative ratio of >1.5 were taken as positive. The evaluation and statistical analysis were done for comparison of the positive/negative ratio in COVID uninfected and infected groups. The number of IgG-positive antibodies subjects was also assessed.

During the vaccination, all subjects were given a pre-structured questionnaire to be filled by themselves for any adverse effect they experienced after the immunization with the Covishield vaccine including the severity, duration, and symptoms for one month after the vaccination. All the study subjects were to report any symptom that could suspect the subject as having a COVID-19 infection. When any subject tested positive for COVID-19, they were immediately isolated and the treatment was given based on the disease severity. For two months following the vaccination, breakthrough COVID infection in healthcare personnel subjects already vaccinated.

The limitation of the study was no comparative assessment with the placebo to assess the efficacy.

The data gathered were analyzed statistically using the SPSS software version 26.0 (IBM, Chicago, IL) and Mann Whitney U test for comparison of the positive/negative ratio and Chi-square test for the efficacy and safety of the vaccine along with the symptom duration. The significance threshold was kept at the p-value of <0.05.

RESULTS

The present prospective analytical study aimed to assess the efficacy, safety, and immunogenicity of the Covishield vaccine in healthcare personnel in India. The study included 244 subjects from both genders that were healthcare personnel. The demographic data of the study participants are summarized in Table 1. The mean age of the study participants was 35.31±6.91 years. The study had 53.27% (n=130) males and 46.72% (n=114) female participants. There were 25.40% (n=62) study subjects that were infected in the present study and 74.59% (n=182) subjects were in the uninfected group of the present study. A positive history of COVID-19 infection was seen in 10.65% (n=26) of study subjects. Among the 244 study subjects in the present study, the majority subjects were nurses with 46.72% (n=114) study subjects followed by 22.13% (n=54) technicians of the institute, 10.65% (n=26) subjects from the billing department, 16.39% (n=40) doctors, 2.45% (n=6) office staff of the institute, and 1.63% (n=4) subjects from the security department respectively as shown in Table 1.

On assessing the seropositivity in the study subjects before and after the Covishield vaccination, the results are summarized in Table 2. It was seen that before vaccination, IgG was positive in 21.31% (n=52) study subjects and negative in 78.68% (n=192) study subjects. Post-vaccination, IgG-positive status was seen in 69.67% (n=170) study subjects and was not seen in 30.32% (n=74) study subjects. In the infected group having 62 subjects, post-vaccination IgG positive was seen in 96.77% (n=60) study subjects and not seen in 3.22% (n=2) study subjects. In the uninfected group including the 182 subjects, post-vaccination IgG positive was seen in 60.43% (n=110) study subjects and was not seen in 39.56% (n=72) study subjects respectively (Table 2).

Concerning the comparison of positive/negative ratio in the study subjects, in the 182 subjects from the uninfected group, the range after 4 weeks was 1.93-4.22 and at 6 weeks was 3.37-6.45 having the test statistic of 3.763 and this was statistically significant with p=0.01. In the infected groups of 62 subjects, the range from pre-vaccination was 2.66-4.52 and the post-vaccination range was 7.55-12.32. The test statistic was 5.795. The difference was statistically significant with p<0.001. Post-vaccination with Covishield, the range in the infected group was 7.55-12.32 which was significantly higher compared to the uninfected group where it was 2.54-5.24 with a statistically significant difference and p<0.001 as shown in Table 3.

For the side-effects in the study subjects after 1st and 2nd doses of Covishield, the most common side-effect seen after the 1st dose was pain at the site of injection reported in 53.27% (n=130) study subjects followed by fever in 27.86% (n=68) study subjects, body ache in 22.95% (n=56) study subjects, headache in 22.13% (n=54) study subjects, giddiness and fatigue in 8.19% (n=20) study subjects each, low backache in 7.37% (n=18) study subjects, and least common was local

swelling seen in 4.91% (n=12) study subjects respectively. After 2nd dose, the most common side-effect was pain at the site of injection seen in 24.59% (n=60) study subjects followed by headache in 12.29% (n=30) study subjects, fever in 7.37% (n=18) study subjects, body ache in 3.27% (n=8) participants, low backache and fatigue in 1.63% (n=4) study subjects each and local swelling in 0.81% (n=2) study subjects respectively. All the side effects had a non-significant difference except body ache which was significantly higher after 1st dose with p=0.02 (Table 4).

DISCUSSION

The mean age of the study participants was 35.31±6.91 years. The study had 53.27% (n=130) males and 46.72% (n=114) female participants. There were 25.40% (n=62) study subjects that were infected in the present study and 74.59% (n=182) subjects were in the uninfected group of the present study. A positive history of COVID-19 infection was seen in 10.65% (n=26) of study subjects. Among the 244 study subjects in the present study, the majority subjects were nurses with 46.72% (n=114) study subjects followed by 22.13% (n=54) technicians of the institute, 10.65% (n=26) subjects from the billing department, 16.39% (n=40) doctors, 2.45% (n=6) office staff of the institute, and 1.63% (n=4) subjects from the security department respectively. These demographics were comparable with the previous studies of Kaur S[9] in 2020 and Lurie N et al[10] in 2020 where for COVID-19, the authors assessed subjects with demographics similar to the present study.

The study results showed that for seropositivity before vaccination, IgG was positive in 21.31% (n=52) study subjects and was negative in 78.68% (n=192) study subjects. Post-vaccination, IgG-positive status was seen in 69.67% (n=170) study subjects and was not seen in 30.32% (n=74) study subjects. In the infected group having 62 subjects, post-vaccination IgG positive was seen in 96.77% (n=60) study subjects and not seen in 3.22% (n=2) study subjects. In the uninfected group including the 182 subjects, post-vaccination IgG positive was seen in 60.43% (n=110) study subjects and was not seen in 39.56% (n=72) study subjects respectively. These results were consistent with the previous studies of Ezgi H et al[11] in 2021 and Merryn V et al[12] in 2021 where the seropositivity before and after vaccination was comparable to the results of the present study.

On comparison of positive/negative ratio in the study subjects, in the 182 subjects from the uninfected group, the range after 4 weeks was 1.93-4.22 and at 6 weeks was 3.37-6.45 having the test statistic of 3.763 and this was statistically significant with p=0.01. In the infected groups of 62 subjects, the range from pre-vaccination was 2.66-4.52 and the post-vaccination range was 7.55-12.32. The test statistic was 5.795. The difference was statistically significant with p<0.001. Post-vaccination with Covishield, the range in the infected group was 7.55-12.32 which was significantly higher compared to the uninfected group where it was 2.54-5.24 with a statistically significant difference and p<0.001. These findings were in agreement with the results of Folegatti Pedro M et al[13] in 2020 and Pimenta D et al[14] in 2021 where authors reported that positive negative ratio results in the subjects affected and not-infected with COVID-19 and before and following vaccination were in line with the results of the present study.

On assessing the side-effects in the study subjects after 1st and 2nd doses of Covishield, the most common side-effect seen after the 1st dose was pain at the site of injection reported in 53.27% (n=130) study subjects followed by fever in 27.86% (n=68) study subjects, body ache in 22.95% (n=56) study subjects, headache in 22.13% (n=54) study subjects, giddiness and fatigue in 8.19% (n=20) study subjects each, low backache in 7.37% (n=18) study subjects, and least common was local swelling seen in 4.91% (n=12) study subjects respectively. After 2nd dose, the most common side-effect was pain at the site of injection seen in 24.59% (n=60) study subjects followed by headache in 12.29% (n=30) study subjects, fever in 7.37% (n=18) study subjects, body ache in 3.27% (n=8) participants, low backache and fatigue in 1.63% (n=4) study subjects each and local swelling in 0.81% (n=2) study subjects respectively. All the side effects had a non-significant difference except body ache which was significantly higher after 1st dose with p=0.02. These side effects were in line with the previous findings of Reynolds CJ et al[15] in 2021 and Anichini J et al[16] in 2021 where the most common side effects following vaccination were fever, pain at the site of injection, fatigue, headache, and body ache.

CONCLUSION

The present study, considering its limitations suggested that the Covishield vaccine has acceptable safety profile levels with increased seropositivity with more intervals in the two doses of the Covishield vaccine. Covishield does not prevent breakthrough infection. However, it can reduce the infection severity of COVID-19.

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TABLES

Characteristics	**Percentage (%)**	**Number (n=244)**
Mean age (years)	35.31±6.91	
Infected group	25.40	62
Uninfected group	74.59	182
COVID infection history	10.65	26
Healthcare personnel		
Doctors	16.39	40
Nurses	46.72	114
Technicians	22.13	54
Office bearers	2.45	6
Billing personnel	10.65	26
Security	1.63	4
Gender		
Males	53.27	130
Females	46.72	114

Table 1: Demographic data of the study participants at the baseline

Variable	**Subgroup**	**%**	**N=244**
Pre-vaccination IgG positive	Yes	21.31	52
	No	78.68	192
Post-vaccination IgG positive	Yes	69.67	170
	No	30.32	74
Post-vaccination IgG-positive infected group (n=62)	Yes	96.77	60
	No	3.22	2
Post-vaccination IgG-positive uninfected group (n=182)	Yes	60.43	110
	No	39.56	72

Tables: Seropositivity in different groups of study subjects before and following the vaccination

Groups		**Range**	**Test statistic**	**p-value**
Uninfected group (post-vaccination) (n=182)	4 weeks	1.93-4.22	3.763	**0.001**
	6 weeks	3.37-6.45		
Infected group (n=62)	Pre-vaccination	2.66-4.52	5.795	**<0.001**
	Post-vaccination	7.55-12.32		
Post-vaccination	Infected group	7.55-12.32	6.524	**<0.001**
	Uninfected group	2.54-5.24		

Table 3: Comparison of positive/negative ratio in different study groups

Side-effects	After 1st dose n (%)	After 2nd dose n (%)	p-value
Low backache	18 (7.37)	4 (1.63)	0.35
Fatigue	20 (8.19)	4 (1.63)	0.44
Body ache	56 (22.95)	8 (3.27)	**0.02**
Local swelling	12 (4.91)	2 (0.81)	0.43
Headache	54 (22.13)	30 (12.29)	0.16
Giddiness	20 (8.19)	2 (0.81)	0.12
Fever	68 (27.86)	18 (7.37)	0.24
Pain at the injection site	130 (53.27)	60 (24.59)	0.08

Table 4: Side-effects after 1st and 2nd dose of Covishield in the study subjects