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Indian Journal of Medical Microbiology 40 (2022) 200–203

Contents lists available at ScienceDirect

Indian Journal of Medical Microbiology

journal homepage: www.journals.elsevier.com/indian-journal-of-medical-microbiology

Original Research Article

Study of immunogenicity, safety and efficacy of covishield vaccine among health care workers in a tertiary cardiac care centre

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ARTICLE INFO

Keywords:
Covishield
Health care workers (HCWs)
Adverse events following immunisation (AEFI)
Seropositivity

ABSTRACT

Purpose: The pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) might be curtailed by vaccination. We assessed the safety, and immunogenicity of Covishield vaccine among Health care workers (HCWs) in a tertiary cardiac care centre.

Methods: It's a prospective analytical study, conducted at Sri Jayadeva Institute of cardiovascular science and research centre, Mysore, between January 2021 to May 2021. Pre and Post vaccination SARS CoV2 IgG antibodies were assessed among 122 HCWs. Interval between two doses in this study were 4 and 6 weeks. Adverse events following immunisation b(AEFI) and efficacy were assessed and followed up for two month post vaccination.

Results: Post vaccination seropositivity was 69.67% in overall study participants. Seropositivity and P/N ratio median value in uninfected and infected group were 60.43% (n = 55),3.47 (IQR: 2.56–5.22) and 96.77% (n = 30),9.49 (IQR: 7.57–12.30) respectively ($P < 0.001$). Seropositivity and P/N ratio after 4 and 6 weeks were 48.3% (n = 60), 2.95 (IQR: 1.91–4.24), and 83.8% (n = 31), 4.88, (IQR: 3.39–6.43) respectively ($P < 0.001$). AEFI after first and second dose was 72.9% and 27.8% ($p < 0.05$) respectively. The most common symptoms after both doses of vaccination were local pain (73% & 88.2%), followed by fever (38.2% & 26.5%). The average duration of symptoms in both doses was 1.75 days. Of 122 participants only 10 (8.19%) had breakthrough infection after two doses of vaccination with mild severity.

Conclusion: Covishield vaccine has showed seropositivity of 69.67%.It has acceptable level of safety profile. Seropositivity and P/N ratio has increased with increase in interval between two doses. Though it has not prevented breakthrough infection it has certainly reduced the severity of infection.

1. Introduction

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has caused a human pandemic of coronavirus disease 2019 (COVID 19). COVID-19 was first reported in November 2019 in Wuhan, China, and subsequently spread worldwide. WHO declared covid19 'A Pandemic' on March 11, 2020. As of July 10, 2021, more than 186 million cases have been confirmed, with more than 4.01 million confirmed deaths [1]. Healthcare workers (HCWs) are at high risk of acquiring infection with COVID-19 resulting in mortality, morbidity, mental stress, disruption of patient care, risk of transmission to patients and family members. Therefore, protection of HCWs from COVID-19 and early detection, isolation and treatment has become a priority worldwide.

Currently there is no specific therapy and vaccine for COVID-19 as it is new to humankind and the nature of protective immune response is poorly understood. It is even unclear that which vaccine strategies will be the most successful. Therefore, it is imperative to develop various vaccine platforms and strategies in parallel. To meet the urgent need for a vaccine, a new pandemic vaccine development paradigm has been proposed that compresses the development timeline from 10–15 years to 1–2 years [2].

Among more than 160 vaccine candidates worldwide, a handful of them entered phase I, II, and III clinical trials [3]. M/s Serum Institute of India, Pune has presented a Recombinant Chimpanzee Adenovirus vector vaccine (**Covishield**) encoding the SARS-CoV-2 Spike (S) glycoprotein with technology transfer from AstraZeneca/Oxford University. After

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https://doi.org/10.1016/j.ijmmb.2022.03.003
Received 7 October 2021; Received in revised form 7 March 2022; Accepted 9 March 2022
Available online 11 April 2022

detailed deliberations, Subject Expert Committee has recommended for the grant of permission for restricted use in emergency situation [4]. Our study aims to assess the immunogenicity, safety and efficacy of Covishield vaccine among HCWs in a tertiary cardiac care centre.

Aims and objective

1) Assessment of antibody response in HCWs following 2 doses of Covishield vaccination
2) Comparison of post vaccination antibody response between covid infected and uninfected HCWs.
3) Comparison of prevaccination and postvaccination antibody response in infected group.
4) Comparison of postvaccination antibody response between 4 and 6 weeks interval between two doses of vaccination in uninfected group.
5) Assessment of overall safety profile following vaccination.
6) Assessment of break through Covid infection in the vaccinated HCWs.

2. Materials and methods

2.1. Study design and participants

A prospective analytical study was conducted at Sri Jayadeva Institute of Cardiovascular Science and Research, Mysuru between January 2021 to May 2021. A total of 122 HCWs of all staff cadre, > 18 years of age were included in the study. Both COVID infected and uninfected staffs were included. Prevaccination screening for SARS CoV2 IgG antibodies was performed. All staff with prior history of covid infection and those who were positive for pre vaccination antibodies were labelled as infected group (n = 31). Staff with no prior antibodies and no history of covid infection were labelled as uninfected group (n = 91). A subgroup of participants delayed the 2nd dose of vaccine by 2 weeks for various reasons; therefore incidentally we had 2 groups who took second dose of vaccine at 4 and 6 weeks interval. Written consent from all the participants and ethical committee approval were obtained.

2.2. Vaccine administration

2 doses of 0.5 ml of COVISHIELD vaccine was administered intramuscularly into deltoid region at the interval of 4 weeks and in subset of the participants at 6 weeks interval.

2.3. Methods

2 ml of blood sample was collected just prior to vaccination and after 28 days of second dose of vaccine. IgG antibodies for SARS CoV2 were assessed using COVID KAWACH IgG MICROLISA Kit (Microwell ELISA test for the qualitative detection of COVID 19 IgG antibodies in serum). The antigen used is SARS CoV 2 virus whole cell antigen coated on to the microtiterplate. Though the kit is recommended for sero surveillance, in this study, Positive to Negative ratio (P/N ratio) which is Sample OD (Optical Density) divided by Mean Negative control, was also determined and analysed comparatively between different groups. Test procedure and interpretation of the result was done according to kit manufacturer's instructions. Sample OD more than cut off and P/N ratio more than 1.5 was considered as positive. Number of participants positive for IgG antibodies before and after vaccination, P/N ratio comparison between COVID infected and uninfected group was assessed and statistically analysed. At the time of vaccination participants were given questionnaires to be filled in if they encountered any Adverse Events Following Immunization (AEFI), which included symptoms, duration and severity observed for a period of one month post vaccination. Participants were instructed to report any symptoms suggestive of COVID infection, if tested positive they were isolated and treated according to severity. Breakthrough covid infection in vaccinated HCWs was observed for a period of two months which coincided with peak of second wave of covid pandemic in India.

2.3.1. Limitation of the study

Control group with placebo could not be included to study the efficacy of the vaccine as no health care worker could be denied of vaccine in the prevalent pandemic situation.

2.4. Statistical analysis

Descriptive statistics is used to present all outcomes, Mann Whitney *U* test is used for P/N ratio comparison. AEFI were analysed using Chi square test and Mann Whitney *U* test used for the comparison of duration of symptoms. A P value less than 0.05 shows statistical significance. Data entered in Microsoft excel and analysed using SPSS version 20.00.

3. Results

Drugs Controller General of India (DGCI) permitted COVISHIELD vaccine for restricted use in emergency situation on January 3rd, 2021. The healthcare workers of Sri Jayadeva Institute of Cardiovascular Science and Research, Mysuru received their first dose of vaccine on January 23, 2021 followed by second dose after 4 week interval, and in a subset of study group at 6 weeks interval. Of 122 sample size 13 participants had past history of covid infection at least 2 months prior to vaccination. Prevaccination screening for IgG antibodies for SARS CoV2 was done in all participants. 26 (21.31%) were tested positive for antibodies. Out of 26 only 8 had previous history of COVID infection, rest 18 had no prior history of covid infection. 5 participants in the infected group were negative for antibodies. After prevaccination screening the total no of participants in the infected group were 31 and 91 were uninfected. We have assessed the baseline characteristics, seropositivity rate to vaccine and P/N ratio in the two groups. In this study population the range of age varied from 19 to 69 years with an average age of 35years. 53% of study group were male [Table 1].

Postvaccination seropositivity for SARS CoV2 IgG antibody was 69.67% in overall study participants. Seropositivity and P/N ratio median value in uninfected and infected group were 60.43% (n = 55), 3.47 (IQR: 2.56–5.22) and 96.77% (n = 30), 9.49 (IQR: 7.57–12.30) respectively (P value < 0.001). The Pre and post vaccination P/N ratio in the infected group was 3.31 (IQR: 2.68–4.54) and 9.49 (IQR7.57–12.30) respectively (P value < 0.001). Seropositivity and P/N ratio after 4 and 6 weeks were 48.3% (n = 60), 2.95 (IQR: 1.91–4.24), and 83.8% (n = 31),4.88, (IQR: 3.39–6.43) respectively (P value < 0.001). [Table 2 and Table 3].

AEFI were recorded in the study population. After first dose, 72.9% participants reported AEFI which reduced to 27.8% following second dose (P value < 0.05).

The most common symptoms after I and II dose of vaccination were local pain (73% & 88.2%), followedby fever (38.2% & 26.5%), myalgia (31.5% & 11.8%), headache (30.3% & 44.1%) respectively. The average duration of symptoms post vaccination in both doses is 1.75 days. Only

Table 1
Baseline characteristics of the study population.

Variables		Frequency	Percentage
Age, (range, Mean ± SD)		19–69 years, 35.33 ± 6.93	
Gender	Male	65	53.30%
	Female	57	46.70%
Designation	Doctor	20	16.40%
	Staff Nurse	57	46.70%
	Technician	27	22.10%
	DEO	3	2.50%
	Group D	13	10.70%
	Security	2	1.60%
H/O Covid Infection	Yes	13	10.70%
Infected group	Yes	31	25.40%
Uninfected group	Yes	91	74.59%

Table 2
Seropositivity among study population.

	Frequency	Percentage
IgG Positive Prevaccination		
Yes	26	21.31%
No	96	78.68%
IgG Positive Post vaccination		
Yes	85	69.67%
No	37	30.32%
IgG Positive Post vaccination in uninfected group(n = 91)		
Yes	55	60.43%
No	36	39.56%
IgG Positive Post vaccination in infected group(n = 31)		
Yes	30	96.77%
No	01	3.22%

Table 3
Comparison of PN Ratio among the study population.

Group	Median	Inter Quartile Range	Test Statistic	P Value
Post vaccination group			6.522	<0.001
Infected	9.49	7.57–12.30		
Uninfected	3.47	2.56–5.22		
Infected group			5.793	<0.001
Pre vaccination	3.31	2.68–4.54		
Post vaccination	9.49	7.57–12.30		
Post vaccination in uninfected group			3.761	0.001
4 Weeks	2.95	1.91–4.24		
6 Weeks	4.88	3.39–6.43		

one participant reported symptoms lasting for more than 7 days. Majority had mild illness in both doses (81.81%) [Table 4, Fig. 1].

Incidence of covid infection over a period of 2 months after vaccination was found to be very less in our study population. Out of the 122 participants only 10 (8.19%) had developed infection after vaccination with mild severity and none among the infected group had Reinfection after vaccination.

4. Discussion

In this prospective analytical study we assessed immunogenicity, safety and efficacy of covishield vaccine. Two doses of covishield vaccine were administered to our HCWs from January to March 2021, as a part of vaccination program by government of India for priority group. Of 122 total study population, 31 were grouped under infected group based on both history of covid infection and presence of prevaccination covid

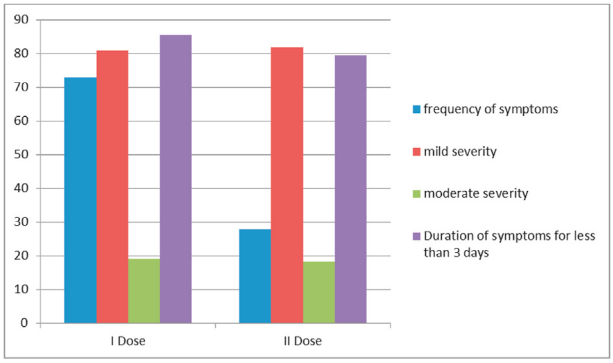

Fig. 1. Frequency of most common AEFI after I and II dose of COVISHIELD vaccine.

antibodies and rest were included in uninfected group (n = 91).

Out of 13 participants who had history of covid infection 8 (61.5%) had IgG antibodies with P/N ratio median value 3.31 (IQR: 2.68–4.54). Different studies have given different rate of seropositivity in covid infected patients. Pyoeng Guyn Choe et al. [5] in their study conducted in South Korea has reported 71% seropositivity in asymptomatic and 100% seropositivity in severe Covid infection after 8 weeks of postinfection. In a similar study by Etienne Brochot et al. [6] out of 151 samples of mild to severe Covid infected cases, seropositivity was 100% for anti RBD, 2 were negative for anti S2. In the same study out of 25 samples of asymptomatic covid positive cases, only 56% were seropositive after 2 weeks of post infection. Therefore the rate of seropositivity after covid infection depends on severity of the disease and duration from the time of infection.

Out of uninfected participants 18 (16.5%) had Prevaccination IgG antibodies, attributing to asymptomatic or mild infection unnoticed. In a seroprevalence study conducted by Tanu Singal et al. [8] in HCWs conducted in a private hospital in Mumbai, seropositivity was 4.3% in asymptomatic and 70% in symptomatic untested participants.

All staff was administered 2 doses of covishield vaccine. Second dose of the vaccine was administered at the interval of 4 weeks (n = 90), 32 participants happened to miss the second dose at 4 weeks but received the dose at 6 weeks. Post vaccination screening for IgG antibodies were done after one month of last dose.

Out of 122 participants 85 (69.67%) were found to have IgG antibodies. In the infected group (n = 31), postvaccination IgG antibodies were detected in 30 (96.77%) participants. One infected participant who was negative for antibodies in prevaccination was found to be negative in post vaccination also. In a similar study conducted by Gabriele Anichini, M.S. et al. [9], one participant out of 100 HCWs was negative for IgG

Table 4
Descriptive assessment of safety profile of the study population.

Side Effects		After first dose		After second dose		P Value
		Yes, n (%)	No, n(%)	Yes, n (%)	No, n(%)	
Local Pain		65 (73%)	24 (27%)	30 (88.2%)	4 (11.8%)	0.072[a]
Fever		34 (38.2%)	55 (61.8%)	9 (26.5%)	25 (73.5%)	0.222[a]
Giddiness		10 (11.2%)	79 (88.8%)	1 (2.9%)	33 (97.1%)	0.149[a]
Headache		27 (30.3%)	62 (69.7%)	15 (44.1%)	19 (55.9%)	0.145[a]
Local swelling		6 (6.7%)	83 (93.3%)	1 (2.9%)	33 (97.1%)	0.416[a]
Body ache		28 (31.5%)	61 (68.5%)	4 (11.8%)	30 (88.2%)	**0.025***[a]
Fatigue		10 (11.2%)	79 (88.8%)	2 (5.9%)	32 (94.1%)	0.371[a]
Low Backache		9 (10.1%)	80 (89.9%)	2 (5.9%)	32 (94.1%)	0.462[a]
Duration, (range, Mean±SD) days		1–15 days, 1.75 ± 1.89		1–10 days, 1.85 ± 2.03		0.795[b]
Duration	<3 Days	76 (85.4%)	5 (5.6%)	27 (79.4%)	7 (20.6%)	**0.021***[a]
	4–7 Days	4 (4.5%)	79 (88.8%)	3 (8.8%)	31 (91.2%)	0.407[a]
	>7 Days	1 (1.1%)	82 (92.1%)	1 (2.9%)	33 (97.1%)	0.511[a]

P < 0.05 shows significance.
[a] Chi square test,
[b] Mann Whitney *U* test,

antibodies following natural infection and vaccination.

In the uninfected group (n = 91), 55 (60.43%), were found to have IgG antibodies postvaccination. The median value of P/N ratio in the infected and uninfected groups were 9.49 (IQR: 7.57–12.30) and 3.47 (IQR: 2.56–5.22) respectively (P value < 0.001). This attributes to booster effect of vaccine in infected group. A similar study by Gabriele Anichini, M.S. et al. [9] has reported significant difference in antibodies titer between infected and uninfected HCWs and reported that after the administration of a single dose of vaccine, the humoral response against SARS-CoV-2 in persons with a history of SARS-CoV-2 infection is greater than the response in previously uninfected participants who have received a second dose. Accordingly Vaccination process stimulates B cell only whereas natural infection stimulates both T cell and B cell, asconcluded by Catherine J. Reynolds et al. [10].

Comparative study between two different intervals between two doses of the vaccine was done in uninfected group only to avoid influence of past natural infection on seropositivity. There was found to be statistically significant difference in the Seropositivity and P/N ratio between two intervals, 48.3%, 2.95 (IQR: 1.91–4.24) and 83.8%, 4.88 (IQR: 3.39–6.43) at 4 and 6 weeks respectively (p < 0.01). Clinical trial group also suggests extended period between two doses [11].

Any vaccine is associated with AEFI, which is a major road block to successful universal vaccine coverage. Our study observed AEFI for a period of one month after each dose. Localized illness like pain, swelling, redness, itching, abscess, weakness and generalized illness such as fever, headache, myalgia, giddiness, low backache, radiating pain, generalized rashes, anaphylaxis, cough, sore throat, and neurological pain were considered as AEFI. Incidence of AEFI after I dose was 72.9% compared to 27.8% after second dose of vaccine (P < 0.05) (Fig. 1).

The most common symptom was local pain after both dose of vaccine, followed by fever in the first dose and headache in the second dose. The trend of symptoms was similar after both doses. Majority of the participants, 85.4% after first dose and 79.4% after second dose had symptoms lasting for less than 3 days, only one participant following both dose complained of symptoms lasting for more than 7 days. The average duration of symptoms post vaccination in both doses is 1.75 days. Majority of the participants had mild illness following both doses. None of them had severe illness or illness requiring admission. In a similar study by Pedro M Folegatti et al. [12], pain was the most common symptom and self-limiting with no major adverse events. Severity being highest on first day after vaccination. Similar study conducted by Merryn Voysey et al. [13] has also demonstrated acceptable safety profile of ChAdOx1 nCoV-19 vaccine.

Post vaccination covid infection was reported by 10 participants with mild severity. None from the infected group had breakthrough infection. Natural immunity followed by booster effect of vaccine has conferred higher protection than vaccine only. With regard to advent of variants of COVID 19 and also non availability of data on waning of COVID antibodies and its clinical implication it is imperative to consider booster dose based on this observation. In a study conducted by Ezgi et al. [14] in a cohort of 417 who had either, Pfizer – Biotech or Moderna vaccine, two women had vaccine breakthrough infection. This observation indicate potential risk of infection even after successful vaccination which emphasizes on importance of covid appropriate behaviour.

5. Conclusion

Covishield Vaccination among health care workers has shown good immunogenicity with a seropositivity rate of 69.67% in overall study participants, and 60.43% in those who had no prior natural infection. Pain is the most common AEFI, lasting less than 3 days with no major adverse events in our study. Seropositivity and P/N ratio has increased with increase in interval between two doses by 2 weeks. Covid Vaccine has shown a booster effect on those who had past natural infection. Booster doses may be considered in future. Though it has not prevented breakthrough infection it has certainly reduced the severity of infection.

Credit author statement

Dr C N Manjunath, Dr Sadananda K S - Conceptualization, Methodology, Dr Ashwini M - Data curation, writing- Original draft preparation, Visualization, Investigation , Supervision, Writing- Reviewing and Editing, Dr Chaithra D - Data curation, writing- Original draft preparation, Writing- Reviewing and Editing.

Funding

Sri Jayadeva Institute of Cardiovascular Science and Research.

Declaration of competing interest

None.

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