Vol. 16(3), pp. 115-120, March 2022
DOI: 10.5897/AJMR2021.9590
Article Number: 477911F68798
ISSN: 1996-0808

http://www.academicjournals.org/AJMR

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African Journal of Microbiology Research

Full Length Research Paper

Antibody responses after Oxford AstraZeneca (Covishield) vaccine among healthcare workers in Dhaka Medical College, Dhaka, Bangladesh

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Received 26 October, 2021; Accepted 23 February, 2022

Oxford AstraZeneca (Covishield) vaccine is the 1st vaccine administered in Bangladesh to prevent the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The antibody response after 1st and 2nd doses of this vaccine was assessed in health care workers of Dhaka Medical College Hospital, Bangladesh. Blood sample was collected from healthcare workers (teachers, clinicians and medical staff) after 28 days of 1st vaccination and 14 days after 2nd vaccination. Quantitative post-vaccination antibody responses were measured using the chemiluminescent immunoassay, ADVIA Centaur (Siemens, Munich, Germany) SARS-CoV-2 IgG (COV2G) assay (output index was ≥1.00). Vaccine related antibody was found in 126 (41%) participants after 1st dose of AstraZeneca vaccine. After 2nd dose of vaccine, reactive level of antibody was found in 172 (93%) participants. Antibody responses were significantly higher in previously infected participants compared to participants who had no history of previous COVID-19 after 1st dose (51.92±50.85 vs 23.67±41.07, p=0.001) as well as 2nd dose of vaccine (64.12±97.76 vs 35.04±64.84, p=0.001). No difference in antibody response was observed among participants with or without comorbidities. Oxford AstraZeneca Covishield vaccine induces a strong immune response after two doses of vaccination.

Key words: SARS-CoV-2, vaccine, comorbidities.

INTRODUCTION

Severe acute respiratory syndrome corona virus type 2 (SARS-CoV-2), which causes the corona-virus-disease-19 (COVID-19) beginning in 2019 in Wuhan, China has rapidly spread throughout the whole world (WHO, 2020). World Health Organization (WHO) has declared COVID-19 as a global pandemic on March 11, 2020 (Del et al., 2020). COVID-19 pandemic has widespread impact on health, including substantial mortality among older adults and those with pre-existing health conditions and impacts on the global economy, caused by physical distancing

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measures, with the greatest consequences for the most vulnerable in society (Zhou et al., 2020). Considering the rapid spread and high mortality of COVID-19, an effective vaccine is urgently needed to control this pandemic. Vaccines can play an important role in increasing population immunity, preventing severe disease, and reducing the ongoing health crisis (Li et al., 2020).

Multiple vaccines have been developed that offer protection against COVID-19 by generating immune responses against the spike antigen of SARS-CoV-2. On the 8 of December 2020, the United Kingdom (UK) started its national vaccination programme with the Pfizer–BioNTech BNT162b2 vaccine (Medicine and Health Care Products, 2020a) followed by the approval of the Oxford-AstraZeneca ChAdOx1 nCoV-19 vaccine, first used outside a clinical trial on the 4 of January 2021 (Medicine and Health Care Products, 2020b). Bangladesh has started its COVID-19 vaccination program in 7th February 2021 with the plans to administer more than 30 million doses over the next few months. The AstraZeneca-Oxford University vaccines, manufactured under license by the Serum Institute of India, had been primarily given to front-line health workers including doctors, nurses and hospital staffs.

Fewer immunogenicity data or comparative data for the Oxford AstraZeneca (Covishield) vaccine are available outside of clinical trials. No study regarding determination of immunogenicity after 1st and 2nd doses of AstraZeneca (Covishield) vaccine has been done yet in Bangladesh. So this study was designed to determine the antibody response among teachers, clinicians and medical staff after 1st and 2nd dose of Oxford AstraZeneca (Covishield) vaccine in Dhaka Medical College.

MATERIALS AND METHODS

Study design and participants

The study was designed to get preliminary idea about vaccine related antibody production. The study was performed in the Department of Microbiology, Dhaka Medical College, Dhaka, Bangladesh. The duration of the study was from February, 2021 to June, 2021. A total of 308 healthcare workers including teachers, clinicians and medical staff of Dhaka Medical College and Hospital, who have taken at least one dose of AstraZeneca Covishield vaccine, participated in this study. Participants who were reverse transcription polymerase chain reaction (RT-PCR) positive for SARS COV-2 infection and recovered were recorded using a data collection sheet. Co-morbidity history of diabetes mellitus and hypertension and history of hospitalization due to Covid-19 were also recorded.

Participants were given Covishield (AstraZeneca vaccine manufactured by Serum Institute of India) in two doses at 8 weeks interval. Side effects after vaccination were noted for all participants.

Blood sample was collected from each participant after 1st and 2nd doses of vaccination. First blood sample was collected after 28 days of 1st vaccination with a window period 7 days and second sample was collected 14 days after 2nd vaccination with a window period of 14 days. Antibody level from the serum was determined using ADVIA Centaur (Siemens, Munich, Germany) SARS-CoV-2 IgG (COV2G) assay, a chemiluminescent immunoassay intended for semi-quantitative detection of IgG antibodies to SARS- COV-2.

According to manufacturer's instructions, serum samples were considered reactive when the output index was ≥1.00 and nonreactive when the output index was <1.00.

All the participants provided written informed consent and the protocol was approved by ethical review committee of Dhaka Medical College.

Statistical analysis

All statistical analysis was performed using IBM SPSS Statistics Version 18 (IBM Co. NY, USA). All variables are presented as means or medians with standard deviation. Categorical variables are shown as numbers with percentages. Student's t test was used to compare between COVID-19 positive participants and non-infected participants. Statistical significance was defined as $p < 0.05$.

RESULTS

In total, 308 participants provided blood specimens and a completed questionnaire for this follow up. Among the participants, 197 (64%) were male and 111 (36%) were female. The mean age was 45.08 years (±9.2 years). Most (61.03%) of the participants were in between 30 and 50 years (Table 1).

In this assessment, 144/308 (46.75%) participants reported no significant medical history and 86 (27.92%) and 51 (16.55%) participants gave the history of hypertension and diabetes mellitus, respectively (Table 1). None of the participants developed complications like blood clotting or other serious adverse effects after vaccination.

Among 308 participants, all the participants gave blood sample after 28 days of 1st dose of AstraZeneca vaccine. After 14 days of 2nd vaccination 185 participants gave blood sample. After 2nd dose of vaccine antibody titre increased in 110 (59.45%) and reduced in 75 (40.54%) participants. Overall antibody titre after 1st dose and 2nd doses were 33.67 ± 46.70, 95% CI: 28.80- 38.65 and 35.40±64.84, 95% CI: 27.50-45.19, respectively.

Out of 308 participants reactive level of antibody was found in 234 (76%) participants after 1st dose of vaccination. Among them, 108 (35.06%) participants were previously COVID-19 positive confirmed by RT-PCR. So vaccine related antibody was found in 126 (41%) participants after 1st dose of AstraZeneca vaccine. After 2nd dose of vaccine out of 185 participants, reactive level of antibody was found in 172 (93%) participants (Table 2).

Out of 108 previously COVID-19 positive participants, blood sample was collected from 62 participants after 2nd dose of AstraZeneca vaccine. These 62 participants, all developed reactive level of antibody after 2nd dose.

In this study, out of 308 participants, 108 (35.06%) COVID-19 positive participants had mild to moderate

Table 1. Demographic status and post vaccination symptoms of participants.

Variable	Total	Percentage
Participants (n)	308	
Male	197	64
Female	111	36
Age (years)		
<30	10	3.25
30-50	188	61.03
>50	110	35.71
Medical history		
Hypertension	86	27.92
Diabetes Mellitus	51	16.55
Bronchial Asthma	10	3.25
Others	9	2.92
Post vaccination symptoms		
Fever	119	38.63
Body ache	133	43.18
Back pain	20	6.49
Vertigo	8	2.59
Headache	7	2.27
Cough	2	0.65
Weakness	3	0.97
Local pain	12	3.89
Allergy	2	0.64
Nausea	3	0.97
Joint pain	2	0.65

symptoms and 31 required hospital admission. These previously infected participants mounted greater antibody response after 1st dose of vaccine compared to participants who had no history of previous COVID-19 infection (51.92±50.85 vs 23.67±41.07, p=0.001) and 2nd dose of vaccine (64.12±97.76 vs 35.04±64.84, p=0.001) compared with previously non-infected participants. No difference in antibody response was observed among participants with or without comorbidities.

DISCUSSION

The ongoing COVID-19 pandemic caused by SARS-CoV-2 has resulted in remarkable mortality and morbidity globally (Krammer et al., 2021). Rapid vaccine-induced population immunity is a key global strategy to control COVID-19 pandemic. Vaccination programs must maximize early impact, particularly with accelerated spread of new variants (Ramasamy et al., 2021).

This study analyzes the antibody response after two doses of Oxford AstraZeneca COVID-19 vaccines in a well-defined group of hospital employees. Until now, limited data has been available looking at antibody response to either a single or double dose of BioNTech/Pfizer or AstraZeneca vaccine in comparison to natural infection or immune-naïve people (Baden et al., 2021).

The data presented by Parry et al., 2021 showed no antibody-response in 13% of individuals after a single dose AstraZeneca in elderly people. In this study, 24% participants were non-reactive after single dose of AstraZeneca vaccine. The reason of lower level of antibody after first dose of vaccination might be due to the fact that, in addition to geographical and ethnic variations, the present vaccine which was used here are produced in serum institute of India and maintenance of cold chain during and after transportation might have some role.

In this study, vaccine related antibody was found in 41% participants 4 weeks after 1st dose of AstraZeneca (Covishield) vaccine. In phases 1 and 2 randomised control trial in humans, one dose of ChAdOx1 nCoV-19 (Covishield) vaccine elicited a significant increase in IgG

Table 2. Antibody response after 1st and 2nd dose of vaccination.

Antibody response	First dose (%)	Second dose (%)
Reactive	234 (76)	172 (93)
Non-reactive	74 (24)	13 (7)

antibodies (91%, peaked by day 28) against SARS-CoV-2 spike protein, as measured by ELISA in 127 participants (Folegatti et al., 2020). Again, a cross-sectional study was done in India among 552 healthcare workers, where 79.3% showed seropositivity after the first dose (Covishield) vaccine (Singh et al., 2021). In another cohort study, 82.1% participants had a positive post-vaccine anti-spike IgG (Wei et al., 2021). The reported higher levels of antibody after 1st dose than the present study might be due to already infected persons were not segregated in those studies. But in the present study, 35% health care workers were already infected before vaccination and were RT-PCR positive and they were not included in calculating antibody response after 1st dose of vaccination. If they were included, total antibody reactivity would be 76%.

In our study after 2nd dose of vaccine, reactive level of antibody was found in 93% participants. Post-vaccination antibody responses were studied in health care workers from Oxford University Hospitals (OUH), four teaching hospitals in Oxfordshire, UK where 97.1% developed a positive anti-spike IgG antibody test by >14 days post-first vaccination and all healthcare workers develop antibody after AstraZeneca second vaccination (Eyre et al., 2021).

There is a broad range of side effects reported after vaccination with BioNTech/Pfizer or AstraZeneca, ranging from local symptoms to systemic post-vaccination symptoms such as fever or headache. These occurred in up to 68.5% of participants after the second dose of BioNTech/Pfizer and up to 58.7% after first dose of AstraZeneca (Menni et al., 2021). In this study, 38.63 and 43.18% participants reported with fever and headache, respectively. There is no correlation between the reported severity of post-vaccination symptoms and immune response measured by antibody levels. Müller et al. (2021) could not find such a correlation either after the first or second dose of BioNTech/Pfizer vaccine.

Menni et al. (2021) reported that the occurrence of side effects is more common in women and in younger people. The majority of participants in this study reported at least one post vaccination symptom, but these reports are not comparable between individuals.

According to world Health Organization (19 April 2021), the AstraZeneca vaccine is safe and effective in protecting people from the extremely serious risks of COVID-19, including death, hospitalization and severe disease. Based on the statement of the WHO Global Advisory Committee on Vaccine Safety on AstraZeneca COVID-19 vaccine, the risk of blood clotting events (Thrombosis with thrombocytopenia syndrome, TTS) with Vaxzevria and Covishield vaccines appears to be very low (WHO, 2021). Data from the UK suggest the risk is approximately four cases per million adults (1 case per 250000) who receive the vaccine, while the rate is estimated to be approximately 1 per 100 000 in the European Union (EU). In our study, no participants reported such type of symptoms after vaccination.

This study demonstrates that previously infected individuals mounted higher immune response after two doses of Covishield vaccines compared with those with no previous infection. Earlier studies reported higher antibody response to a single dose of vaccine in previously infected individuals (Rinott et al., 2021). The immune response to the vaccine after the first dose is substantially pronounced in individuals with pre-existing immunity and it is similar to the immune response developed after the second dose in individuals not previously infected (Krammer et al., 2021). The reason behind it might be due to the fact that memory cells are developed in individuals after natural infection and the memory cells are stimulated by the first dose of vaccine and produce more antibodies. In a related UK-wide study and a study from Israel, high levels of protection from infection following natural infection were observed that were comparable to those seen after two doses of vaccination without prior infection (Pritchard et al., 2021; Goldberg et al., 2021).

In this study, after 2nd dose of vaccination antibody titer were reduced from titer observed after 1st dose in 75 (40.54%) participants. Exact cause of this phenomenon is unknown. The reason of decreased antibody titer after 2nd dose than 1st dose might be due to antivector antibody was formed after 1st dose which neutralized the vaccine vector after 2nd dose. Another reason might be during the study period, high infection rate was prevailing in Dhaka city, the participants might have been contracted with the virus within few days prior to collection of blood after 2nd vaccination and the viruses might have neutralized the antibodies produced after 1st dose. Substantial level of antibodies was produced among the participants who received two doses of AstraZeneca (Covishield) vaccine.

Conclusion

The Oxford AstraZeneca (Covishield) vaccine produced

significant levels of antibodies among doctors and other staffs without any severe adverse events.

Limitations

Participants were not followed up whether they got infected with SARS-cov2 virus who developed reactive level of antibodies.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

ACKNOWLEDGMENTS

The authors acknowledge the Office of the Director General of Health Services (DGHS), Bangladesh for financial support and thank all the participants who volunteered for this study. They sincerely thank Principal Professor Dr. Md. Titu Miah and vice Principal Dr. Md. Shafiqul Alam Chowdhury of Dhaka Medical College, Dhaka, Bangladesh for their active cooperation.

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