

ORIGINAL ARTICLE

ANTI-COVID ANTIBODY STATUS IN HEALTH CARE PROFESSIONALS OF BANGLADESH AFTER 3 MONTHS OF COMPLETION OF TWO DOSES OF COVID-19 VACCINATION

AYATUN NESA¹, KAZI MUHAMMAD MAHBUBUR RAHMAN², ABDUL ALI³, ROKSANA YESMIN⁴

Abstract

Background: Coronavirus 2019 (COVID-19) is a pandemic disease, where huge number of populations was infected, and massive death occurred worldwide for its rapid spread. Naturally produced antibody or artificially given vaccination can only give protection. This study evaluated the anti-Covid antibody status in health care professionals of Bangladesh after 21 days and 3 months of completion of two doses of Covid-19 vaccination. **Methods:** This study was conducted at the Department of Laboratory Medicine, BIRDEM, Dhaka. Total 100 respondents who had completed two doses of Covid-19 vaccination were enrolled according to inclusion criteria. After taking informed written consent a structured questionnaire was filled up for each subject. First sample (3 ml whole blood) was collected after 21 days of completion of 2nd doses of SARS-CoV-2 vaccination and a 2nd sample (3 ml whole blood) was collected again after 3 months. SARS-CoV-2 IgG was estimated by indirect chemiluminescence assay. Collected data were analyzed by SPSS 22. **Results:** The mean age of the study subjects was 32.09 ± 7.98 . Study subjects were divided into two groups: those with history of past Covid infection (PCR positive) (n=33) and those with no evidence of past infection (n=67). SARS-CoV-2 IgG antibody level was found significantly reduced after 3 months of completion of vaccination, compared to the titer of 21 days of vaccination. A significant difference of mean SARS-CoV-2 IgG antibody level among subjects with and without previous history of Covid 19 infection was observed after 21 days of completion of 2nd dose of Covid 19 vaccination. However, after 3 months of 2nd dose of vaccination no significant differences of mean SARS-CoV-2 IgG antibody level were observed between the groups. **Conclusion:** SARS-CoV-2 IgG antibody level was significantly reduced after 3 months of completion of two doses of vaccination. Moreover, antibody level was found significantly higher among the study subjects with previous positive H/O of Covid 19 infection compared to subjects without any H/O previous Covid infection. Therefore, this study recommended that, a third booster dose would be necessary to maintain the effectiveness of vaccines.

Key words: Covid-19 vaccination, SARS-CoV-2 IgG antibody

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1. Professor, Dept. of Laboratory Medicine, BIRDEM General Hospital, Shahbag, Dhaka-1000, Bangladesh.
2. Senior Medical Officer (Ex.), Department of Laboratory Medicine, BIRDEM General Hospital, Shahbag, Dhaka-1000, Bangladesh.
3. Research Assistant, Anti COVID Antibody Project, Ministry of Science & Technology (2021-2022), Dhaka-1000, Bangladesh.
4. Associate Professor, Department of Biochemistry, Ibrahim Medical College, Segunbagicha Dhaka-1000, Bangladesh.

Address of Correspondence: Prof. Dr. Ayatun Nesa, Professor, Dept. of Laboratory Medicine, BIRDEM General Hospital, Shahbag, Dhaka-1000, Bangladesh. Email: dipa2801@yahoo.com

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Introduction:

Coronavirus is an enveloped single stranded RNA virus of Coronaviridae family and Orthocoronaviridae subfamily.¹ Severe acute respiratory syndrome coronavirus-2 (SARS -CoV-2), causative agent of Coronavirus disease 2019 (COVID-19) is a pandemic situation faced by the world. The World Health Organization (WHO) declared a Public Health Emergency on January 30, 2020, after COVID-19 had spread to other countries (Casella et al., 2020) and declared COVID-19 a pandemic in March 2020 (WHO, 2020).² According to the Institute of Epidemiology, Disease Control and Research (IEDCR) (22 March 2020), Bangladesh is the second most affected country in South Asia, after India.³ Fever, cough, loss of smell sensation, shortness of breath are the most common symptoms. In addition, gastrointestinal manifestations such as nausea, vomiting, anorexia, diarrhoea, and abdominal pain are more clinical manifestations.⁴

COVID-19 has four structural proteins: spike (S), envelope (E), membrane (M), and nucleocapsid (N) proteins. Receptor-binding domain (RBD) of the spike protein acts as an antigen for identification of immune reactions.⁵ Transmission of COVID-19 occurs through respiratory droplets. The spike protein facilitates viral entry into host cells firstly by binding to a host receptor through the RBD in the S1 subunit and afterward fusing the viral and host membranes through the S2 subunit. Antibodies binding to the spike (S) protein RBD can neutralize SARS-CoV-2.⁵

Body immune system responses to a pathogen with both innate and adaptive immunity. One aspect of the adaptive immunity is humoral response that features the production of antibodies recognizing specific antigens.⁶ Several follow-up studies of hospitalized patients in Sweden had reported about the development of IgG in majority of patients.⁷ A prospective study in Korea investigated antibody production in asymptomatic and mild COVID-19 patients and reported that neutralizing antibodies production was significantly lower in asymptomatic to mild symptomatic patients, compared to that of moderate to severe patients with pneumonia.⁸ But non hospitalized home treated patients developed antibodies by days 21–28, with a significant lower titer.⁹ In Southeast Asia, a cross-sectional study in India reported IgG antibodies appeared two weeks after infection and are sustained high for long time.¹⁰ The presence of anti-spike or anti-

nucleocapsid IgG antibodies was associated with a substantially reduced risk of SARS-CoV-2 reinfection in next 6 months.¹¹

Vaccine against SARS -CoV-2, offer great promise for curbing the spread of COVID-19 infection. Since the vaccines have been developed, other important questions must be addressed, including the durability of protection over a long period after vaccination and the determination of the effect of a booster dose to extend the duration of immunity against SARS-CoV-2 infection. Bangladesh began administration of COVID-19 vaccines on 27 January 2021 while mass vaccination started on 7 February 2021.^{12,13} However, there are limited ideas about the duration of persistence of antibody after infection or vaccination. So, this study was done to know the quantitative antibody titer among the health care professionals who had completed two doses of SARS-CoV-2 vaccine.

Methods:

After taking informed written consent, a total 100 health care professionals, who had received both doses of the Covid 19 vaccination, were included according to inclusion criteria. This observational cohort study was conducted in the department of Laboratory Medicine, BIRDEM General Hospital, Dhaka. After taking informed written consent from each study subjects, a preset questioner had been filled up. All the base line characteristics along with personal history, clinical history, clinical examination findings and relevant investigation findings were included in the preset questioner. First sample (3 ml of venous blood in plain tube) was collected after 21 days of completion of 2nd doses of SARS-CoV-2 vaccine and a 2nd sample (3 ml of venous blood in plain tube) was collected again from each study subject after 3 months of 2nd dose of SARS-CoV-2 vaccination. Serum was separated after centrifugation on the same day of sample collection. The serum samples were stored at -80 degree Celsius till the antibodies were measured. SARS-CoV-2 IgG was estimated by indirect chemiluminescence assay. Statistical analysis was performed with the help of Statistical Package for Social Science 23, (SPSS 23) version. Descriptive statistics were presented as mean±SD score for normally distributed data. Continuous data were compared using parametric test (Student's unpaired t-test, ANOVA, Chi square test). Statistical tests was considered significant at the level of $p < 0.05$ and considered as test of significance when $P < 0.05$.

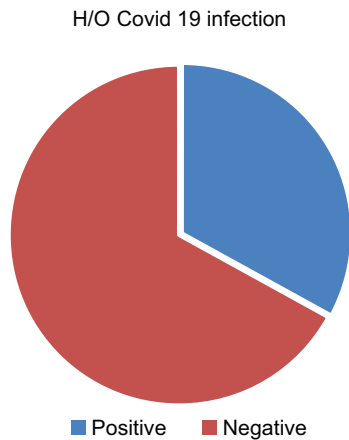


Fig.-1: Distribution of the study subjects according to previous history of PCR positive Covid 19 infection

Results:

Table 1 shows the baseline characteristics of the study subjects. The mean age of the study subjects was 32.09 ± 7.98. The study subjects were categorized into four different age group categories (<30, 31-40, 41-50, and 51-60 years) and majority (48%) of the study subjects were belong to 31-40 years age group (Figure 2). Mean BMI of the study subjects was 25.40 ± 2.82. In this study, among the health care professionals, 32% were Physician, 26 % Nurse/ Midwife, 8% Administrative Officer, 15% Cleaning staff and 19% were of other staffs. 32% study subjects were smokers (Table 1).

Table I

Baseline Characteristics of the Study Subjects

Variable	Total (n=100)
Age (years)†	32.09 ± 7.98
BMI (kg/m²)†	25.40 ± 2.82
Sex, n (%)	
Male	45
Female	55
Occupation, n (%)	
Physician	32
Nurse/ Midwife	26
Administrative Officer	08
Cleaning staff	15
Others	19
H/O Smoking, n (%)	
Yes	30
No	70

† Values are Mean ± SD; BMI: Body mass index

Study subjects were divided into two groups: those with history of past Covid infection (PCR positive)(n=33) and those with no evidence of past

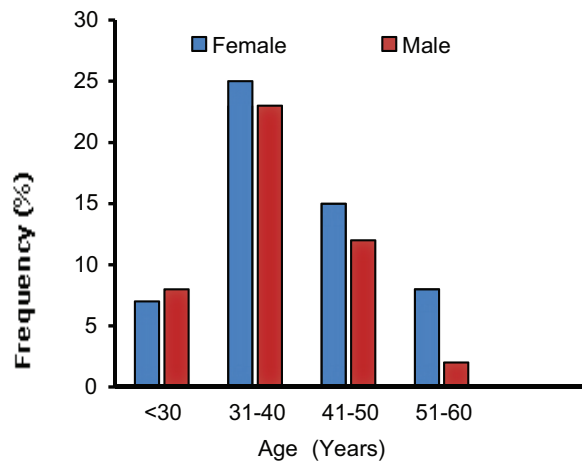


Fig.-2: Frequency Distribution of Study Subjects according to different Age Group

infection (n=67) (Figure 1). Table 2 presents the demographic features of study subjects according to previous Covid 19 infection history. The mean age of subjects with and without previous H/O Covid infection were 36.67±8.59 and 29.84±6.64 respectively. There was significant difference in between the mean age of two groups. The mean BMI were 26.93±3.52 and 25.66±3.60in subjects with and without previous Covid 19 infection, respectively, but no significant differences were observed. In this study, among the subjects with previous H/O covid 19 infection 39.4 % were male and 60.6% were female. Moreover, 57.6 % of subjects with previous H/O Covid 19 infections were smoker.

Table II

Demographic features of study subjects according to the history of previous Covid 19 infection

Variables	Previous H/O Covid 19 infection	No Previous H/O Covid 19 infection
Mean age (yrs) †	36.67±8.59	29.84±6.64*
BMI (yrs) †	26.93±3.52	25.66±3.60
Sex, n (%)		
Male	13(39.4)	32 (47.8)
Female	20 (60.6)	35 (52.2)
History of smoking, n (%)		
Yes	19 (57.6)*	11 (16.4)
No	14 (42.4)	56 (83.6)

† Values are Mean ± SD; *p<0.05 was taken as the level of significance

SARS-CoV-2 IgG antibody level after 21 days of 2nd dose of vaccination, among the subjects was 1622.63 (115.0-11525.4) and after 3 months of vaccination was 1151.12 (44.2-6617.5). It was found that, SARS-CoV-2 IgG antibody level was significantly reduced after 3 months of completion of vaccination, compared to the titer of 21 days of vaccination.

Table III

Comparison of SARS-CoV-2 IgG antibody level among the study subjects after 21 days and 3 months of completion of 2nd dose of Covid 19 vaccination

	21 days after 2 nd dose of Covid 19 vaccination	3 months after 2 nd dose of Covid 19 vaccination
SARS-CoV-2 IgG antibody level (AU/ ml) †	1622.63 (115.0-11525.4)	1151.12* (44.2-6617.5)

† Values are Median (min-max); * $p < 0.05$ was taken as the level of significance

Table IV

SARS-CoV-2 IgG antibody level after completion of 2nd dose of Covid 19 vaccination according to previous H/O Covid 19 infection

	Previous H/O Covid 19 infection	No Previous H/O Covid 19 infection
SARS-CoV-2 IgG antibody level (AU/ ml)		
After 21 days of 2 nd dose of Covid 19 vaccination †	1945.3	1463.7*
After 3 months of 2 nd dose of Covid 19 vaccination †	1377.5	1039.6

† Values are Mean; * $p < 0.05$ was taken as the level of significance

A significant differences of the mean SARS-CoV-2 IgG antibody level after 21 days of completion of 2nd dose of Covid 19 vaccination (1945.3 AU/ml and 1463.7 AU/ml) were observed among subjects with and without previous history of Covid 19 infection (Table IV). However, the mean SARS-CoV-2 IgG antibody level after 3 months of 2nd dose of vaccination were again estimated among the two groups but there was no significant differences were observed (Table IV).

Discussion:

The general regime in the vaccination against COVID-19 is administering the vaccines in two doses. This study aimed to measure the level of anti-SARS-CoV-2 IgG antibodies in health care professionals, who had completed 2nd dose of COVID-19 vaccination. The results of this study suggested two main outcomes: one is, anti-SARS-CoV-2 IgG antibody responses were significantly higher among the healthcare professionals with previous history of Covid infection compared to without history of any Covid infection. Another finding is, three months after a two-dose vaccination regime, anti-SARS-CoV-2 IgG antibody responses were relatively low compared to previously reported levels.

In this study, median (Inter Quartile Range, IQR) SARS-CoV-2 IgG antibody level were estimated after 21 days and 3 months of 2nd dose of vaccination, among the study subjects. It was found that, SARS-CoV-2 IgG antibody level was significantly reduced

after 3 months of vaccination, compared to the titer of 21 days of vaccination. Bayram et al. investigated SARS-CoV-2 anti-spike antibodies in 1012 Turkish health care workers (HCWs) after two doses of CoronaVac (Sinovac). Antibodies were detected in 1008 of 1012 (99.6%) HCWs, 21 days after the second dose, and the median antibody titer of HCWs was calculated as 1022.40 AU/ml (range: 10.10–66 923.70 AU/ml).¹⁴ Yigit et al. investigated 678 Turkish HCWs 2 months after the second dose of CoronaVac using a semiquantitative method deployed a recombinant protein to represent the nucleocapsid (N) antigen of the virus (Elecsys Anti-SARS-CoV-2; Roche) and found titer in all participants after approximately four and a half months after the vaccination with a two-dose regime of CoronaVac before the vaccination with the third booster dose was 175.7 AU/ml (min: 10.90 AU/ml, max: 5201.60 AU/ml) and 11% of the participants were seronegative supporting the idea that antibody titers decrease over time sometimes in the degree of patients being seronegative.¹⁵ In a recent study, Yue et al. reported antibody titers fading after inoculation with two doses of an inactivated SARS-CoV-2 vaccine in a cohort of 355 volunteers participating in the development and production of inactivated vaccines. At 3 months after the second dose, the serum neutralizing antibody titers in this cohort decreased significantly. Their results suggested that a third booster dose was necessary to maintain the effectiveness of inactivated vaccines regardless of sex and two-dose immunization procedure.¹⁶

SARS-CoV-2 IgG antibody level were observed among the two groups of study subjects (subjects with and without previous history of Covid 19 infection). The mean SARS-CoV-2 IgG antibody level after 21 days of completion of 2nd dose of Covid 19 vaccination were estimated in this study and significant differences were observed between the groups. However, the mean SARS-CoV-2 IgG antibody level after 3 months of 2nd dose of vaccination were again estimated among the two groups but there was no significant differences were observed. A recent study investigated quantitative SARS-CoV-2 anti-spike responses to two doses of BNT162b2 using Abbott's assay and reported median IgG SP titers of 10 058 (6408–15 582) AU/ml in cases without evidence of previous infection and 18 047 (10 884–22 413) AU/ml in cases with known previous infection.¹⁷ Soysal et al. analyzed immunogenicity and reactogenicity of inactivated SARS-CoV-2 vaccine (CoronaVac) in both previously SARS-CoV-2 infected and uninfected Turkish HCWs and reported median SARS-CoV-2 IgG antibody levels of 1220 AU/ml (range: 202–10 328 AU/ml) and 913 AU/ml (range: 2.8–15 547 AU/ml) 28 days after the second vaccination in infected and uninfected HCWs, respectively.¹⁸

Conclusion:

In present cohort study, anti-SARS-CoV-2 IgG antibody responses after completion of 2 doses of vaccination were found significantly higher among the health care workers with previous history of Covid infection compared to without history of any Covid infection. It was also found that, three months after a two-dose vaccination regime, anti-SARS-CoV-2 IgG antibody responses were relatively low compared with previously reported levels.

Limitations:

This study was conducted in a single center with limited time of span with a smaller number of samples. Primary antibody level, before vaccination could not be measured. Subject with might had natural infection but had not undergone for PCR test could not be differentiated properly. Antibody responses according to different vaccine regime also could not be evaluated in this study. So, further prospective study with large sample size with long duration should be done. A third booster dose will be necessary to maintain the effectiveness of vaccines regardless of sex and two-dose immunization procedure.

Conflict of Interest:

There is no conflict of interest in this study

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Ethical consideration:

The study was conducted after approval from the ethical review committee. The confidentiality and anonymity of the study participants were maintained

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