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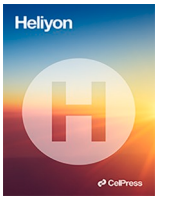

SARS CoV-2 IgG positivity among the people in Dhaka city: An observation from the post vaccine period

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ABSTRACT

Immunity status after mass vaccination program against SARS CoV-2 has not been evaluated in Bangladesh. This study aims to assess the IgG response against SARS-CoV-2 among the vaccine receivers in Bangladesh. After signed consent, blood samples were tested for SARS CoV-2 IgG from volunteers between March, 21 and April, 22 using ELISA where IgG index $\geq$0.9 was considered as positive Among 3034 participants, IgG positivity was calculated approximately 82% for vaccine recipients; lowest (58%) during March–April, 21 which increased to 85–95% later. IgG positivity and mean index was 82% and 3.04 in vaccinated whereas 56% and 1.5 in unvaccinated cases. IgG positivity and mean index reduced with age: 90% and 2.56, 79% and 2.23, 73% and 2.13 in 18–40 y, 41–60 y, >60 y group respectively. Vaccinated with COVID-19 history showed highest IgG positivity and index (94% and 3.1) compared to vaccinated without COVID-19 history (76% and 1.6), unvaccinated with COVID-19 history (75% and 1.5) and unvaccinated without COVID-19 history (51% and 0.9). IgG positivity and index reduced as interval between IgG testing and vaccination increases. Our findings suggest a robust IgG response among the vaccine recipients. Negative correlation of IgG positivity and index with age and time necessitates continuous monitoring of immunity status.

1. Introduction

COVID-19 pandemic has created havoc around the world, not only in terms of deaths [1] but also in people's lives by disruption of health services and global economy. Though various policies regarding the reduction of transmission have already been imposed all around the world to minimize the burden, the ultimate solution to this pandemic known so far is the achievement of immunity among the people through mass vaccination. Till date, 21 vaccines have been officially launched [2] and distributed throughout the world with 349 more in the pipeline: 153 in the clinical and 196 in the pre-clinical trial [3].

However, the mass vaccination is still a stiff challenge as there are issues regarding the supply chain management, cost and variation in efficacy among vaccines. Because of the limited resources, the public health policies should ensure that the policies are designed in such a way that the vaccine doses can be best utilized. Such policies like identifying high risk group and prioritize that for vaccination, administration of one dose as many people as possible rather than providing 2nd dose to a part of the population, mixing

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and matching of different COVID-19 vaccines, the persistence of antibody in the body to identify the requirement of booster doses etc. demands more public health research.

Bangladesh introduced mass COVID-19 vaccination on 7th February 2021 [4]. So far, the country has approved 7 vaccines and altogether administered 128,514,470 and 116,139,241 of first and second dose of vaccines which covered almost 70% of total population and achieved the WHO target. Till now, the country administered altogether 12,267,559 dose (approximately 10.56%) of 3rd dose [5]. Like other countries in the world, Bangladesh started vaccination with the older age group of the population and recently the country started vaccination among the teenage group. However, the immunity status against COVID-19 among the mass people has not been assessed since the vaccines have been introduced. This study, therefore, aims to i) assess the antibody (IgG) response against SARS-CoV-2 among the vaccine receivers in Bangladesh, ii) compare SARS CoV-2 antibody (IgG) response among vaccine recipients with non-vaccinated cases and different age groups iii) whether SARS CoV-2 IgG among the IgG positive cases reduced with time.

Table 1
Baseline characteristics of the study participants.

Characteristics		Frequency (%)
Number of participants		3034
Age, Mean (min,max)		41.7 (5-75 y)
Male		2183 (72%)
Blood group		
	A+	564 (18.6%)
	B+	857 (28.2%)
	O+	769 (25.3%)
	AB+	237 (7.8%)
	Others	91 (3%)
	Missing	516 (17%)
Weight, Median (min,max) (kg)		68 (23–137)
Previously RT PCR positive		520 (17%)
COVID-19 severity		
	Asymptomatic	125 (4.1%)
	Mild	201 (6.7%)
	Moderate	195 (6.4%)
	Severe	30 (1%)
Vaccination		
	One	472 (15.6%)
	Two	1675 (55.2%)
	Three	53 (1.7%)
	Missing	55 (1.8%)
	Unvaccinated	779 (25.7%)
Vaccine brand		
	Astrazeneca	1574 (51.3%)
	Verocell	489 (15.9%)
	Moderna	59 (1.9%)
	Pfizer	58 (1.8%)
	Others	4 (<1%)
	Combination of vaccines	21 (<1%)
Comorbidities		
	Asthma	76 (2.4%)
	Diabetes	138 (4.5%)
	High blood pressure	207 (6.8%)
	Low blood pressure	24 (<1%)
	Neprological complications	19 (<1%)
	Hepatological complications	20 (<1%)
	Cancer	4 (<1%)
	HIV	0 (0%)
	Jaundice	3 (<1%)
	Dengue history	43 (1.4%)
	Anemia	19 (<1%)
Symptoms		
	Fever	90 (2.9%)
	Cough	80 (2.6%)
	Breathing difficulties	76 (2.5%)
	Loss of smell	67 (2.1%)
	Lethargy	82 (2.7%)
	Loss of taste	67 (2.2%)
	Dizziness	67 (2.2%)
	Sore throat	65 (2.1%)
	Headache	74 (2.4%)
	Body ache	68 (2.2%)
	Diarrhea	65 (2.1%)
	Vomiting	66 (2.2%)

2. Results

A total of 3034 participants were enrolled in the study. Of these, 2205 were vaccinated and 779 were not vaccinated. Out of the 2205 vaccinated cases, 472 had single dose, 1675 had two dose and 53 had three doses of vaccines from different manufacturers. The mean age of the participants and the standard deviation were 41.6 and 14.5 respectively. Twenty seven percent of the participants were female. The baseline characteristics of the participants are shown in Table 1.

The seropositivity of IgG positivity was calculated approximately 82% for recipients of the vaccine. IgG positivity was lowest during Mar, 21 and Apr, 21 (approximately 58%) which increased and remains constant (between 85 and 95%) during the later period (Fig. 1). During the same time period national data regarding the SARS CoV-2 positivity rate were collected (http://dashboard.dghs.gov.bd/webportal/pages/covid19.php) and compared with the IgG positivity of the study. Though there was a surge of SARS CoV-2 positivity in April, 21, June–Aug, 21 and Jan–Feb, 22, no correlation was found between the national SARS CoV-2 positivity rate and IgG positivity data from our study. The seroprevalence among unvaccinated individuals was estimated to be 56%. Additionally, the level of IgG was significantly higher in two/three dose vaccinated cases compared to unvaccinated cases (mean IgG index: 3.04 vs 1.5) and when the IgG level is compared within vaccinated cases two/three dose vaccinated cases showed higher seropositivity and IgG level compared to single dose vaccinated cases (Table 2).

To identify whether the IgG positivity and IgG index changes with age, we identified 658 cases that were negative by RT PCR, received two dose vaccines, IgG was analyzed within 21–28 days and age was available. The seropositivity among 18–40 y, 41–60 y and >60 y was found 90%, 79% and 73% respectively. IgG level also showed a reduction with age: 2.56 in 18–40 y, 2.23 in 41–60 y and 2.13 in >60 y age group. When compared with 18–40years age group, IgG positivity and IgG index was found significantly lower in 41–60 y and >60 y age group (Table 3).

To understand the IgG level further we categorized cases as the following groups: 1) RT PCR positive two/three dose vaccinated cases, 2) RT PCR negative two/three dose vaccinated cases, 3) RT PCR positive unvaccinated cases and 4) RT PCR negative unvaccinated cases. IgG positivity was found 94%, 76%, 75% and 51% respectively. Median IgG level among these four groups was found 3.1, 1.6., 1.5 and 0.9 respectively. Compared to Group 1, both the IgG positivity and mean IgG index were found significantly lower in other groups (Fig. 2).

To identify whether there is any effect of time interval between last vaccination date and IgG test date with the seropositivity and IgG level, we selected a cohort of 1305 cases. When the cohort is adjusted for age, the median IgG among all the age group showed a decreasing trend as the time interval between last vaccination date and IgG test date increases. However, the level of reduction varied with different age group (Fig. 3).

3. Discussion

Overall, we found IgG positivity among the participants who received vaccination was 82%. However, except for the Month of March–April, 21, the first two months after the vaccination program being launched in the country, the IgG positivity was between 85 and 95%.This is consistent with other studies around the world [6–10]. When compared with the national SARS CoV-2 positivity rate, we found no correlation with the IgG positivity indicating the increased IgG positivity since April, 21 was due to the mass vaccination rather than a surge in the SARS CoV-2 positivity. When compared, the level of IgG was found higher in double dose vaccinated participants compared to the single dose recipients. As earlier studies have shown that higher IgG titer corresponds higher neutralizing antibody titer [11,12] and higher neutralizing antibody renders better protection [13], it can be assumed that the higher level of IgG

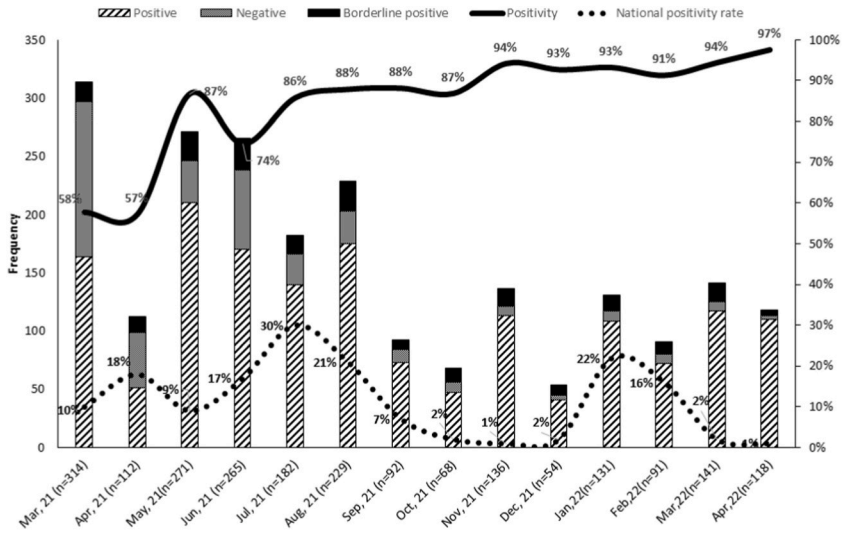

Fig. 1. Month wise seropositivity among vaccinated cases (n = 1723).

Table 2
Dose wise SARS CoV-2 IgG positivity and level.

Vaccination status	Frequency	IgG positive cases	Sero-positivity	p-value	Mean IgG index (range)	p-value
Vaccinated	2200	1797	82%	<0.05	3.04 (0.1–16)	<0.05
Single dose	472	296	63%		2.2 (0.1–10.4)	
Two dose	1675	1449	86.5%		3.2 (0.3–12.0)	
Three dose	53	53	100%		5.8 (0.9–16.0)	
Un-vaccinated	779	326	55%		1.5 (0.1–9.9)	

Table 3
Comparison of SARS CoV-2 IgG positivity and level among different age groups.

Age category	Frequency	No. IgG positive cases	Sero-positivity	p-value	Mean IgG index (range)	p-value
18–40 y	273	246	90%	ref	2.56 (0.3–10.4)	ref
41–60 y	271	214	79%	<0.05	2.23 (0.3–8.8)	<0.05
>60 y	114	83	73%	<0.05	2.13 (0.2–8.6)	<0.05

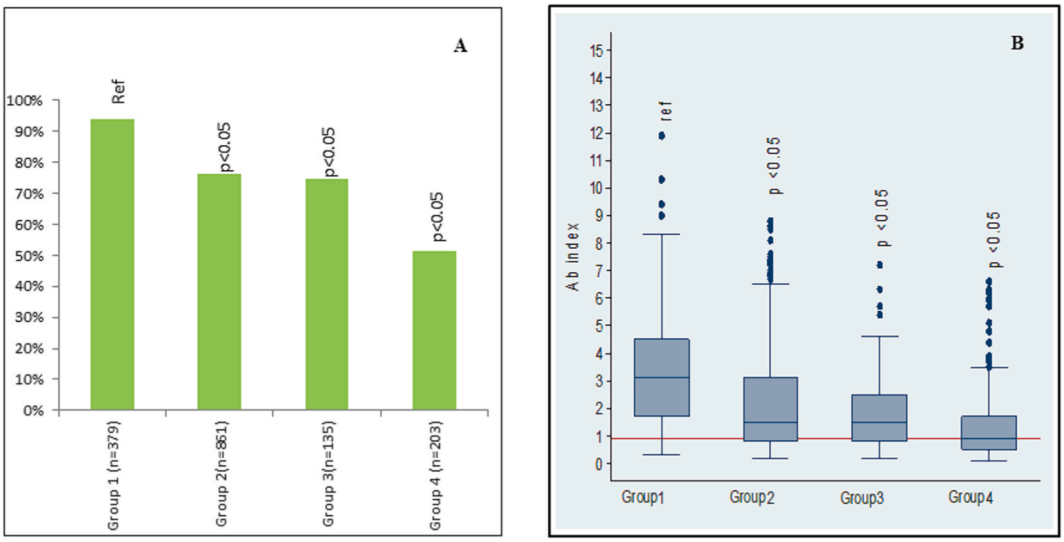

Fig. 2. SARS CoV-2 IgG A) seropositivity and B) level among various groups: i) Group-1 (RT PCR positive two dose vaccinated cases) ii) Group-2 (RT PCR negative two dose vaccinated cases) iii) Group-3 (RT PCR positive unvaccinated cases) iv) Group-4 (RT PCR negative unvaccinated cases).

among the participants after vaccination might render protection against COVID-19 despite neutralizing antibody titer has not been performed in the study. A further investigation revealed that for the first two months the duration between vaccination and serological testing was less than 21 days (median 14 days). This might be too early to detect an IgG response as the IgG reaches highest level between 21 and 28days after vaccination or COVID-19 infection [14,15]. The duration between vaccination and serological testing was between 21 and 28 days (Median 25 days) for the other months.

Our study also showed that the IgG positivity and the level of IgG were lower among the older age group compared to the younger age group. This is in consistence with other studies [16,17] where neutralizing antibody titer was found lower in elderly participants compared to younger participants. Though in our study, we did not perform the neutralizing antibody titer, a strong established correlation between IgG and neutralizing antibody allowed us to assume the similar correlation with the IgG. Indeed, a negative relationship between IgG titer and age was reported by other studies [18].

We found that the highest IgG positivity and IgG level was found among the participants who reported previous infection and two/three dose vaccinated followed by two/three dose vaccinated without previous infection, not vaccinated with previous infection and not vaccinated with no infection reported. Similar results were reported by other studies [7,19].

We also investigated whether there is any effect of duration of serological testing and vaccination on the IgG level across all age group. All the age group showed gradual decline of the median IgG level as the duration between vaccination and IgG testing increases after one month of vaccination. This indicates a reduction of IgG level with time which further corporates the booster dose campaign launched by the country. In our study, when we used linear regression to all age group and also to the specific age group, we found that after 6months or more from the 2nd dose of vaccination the IgG titer reduce by approximately 1.5 times and just above the threshold level of detection. Naaber et al. found that the IgG level reduced to 7% of their peak after six months from the 2nd dose of vaccination

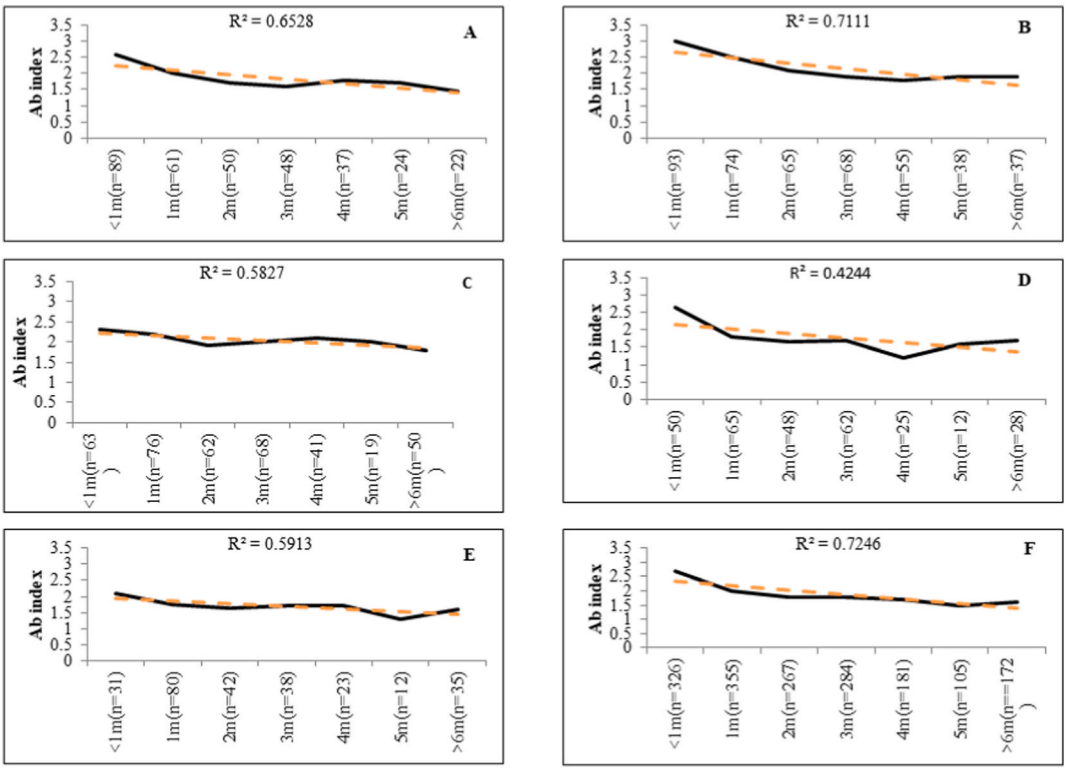

Fig. 3. Decline of IgG level with time interval between vaccination and serological test date of different age groups: A) ≥30 y, B) 31–40 y, C) 41–50 y, D) 51–60 y, E) >60 y, F) all age.

[18].

The study has several limitations. The participants were enrolled voluntarily and it was a single centered study. Additionally, we could not analyze IgM for SARS CoV-2, neutralizing antibody and sequential sample to have a better understanding of the IgG dynamics with time. We also could not follow up the participants to determine the relationship between IgG positivity and titer with protection against SARS CoV-2 infection.

4. Conclusion

This study was one of the initial studies of assessing the IgG response against various types of commercially available vaccines among the people in Dhaka city during post vaccination period. The findings from the study showed that there is a robust IgG response among the vaccine recipients. However, the IgG response was higher after two dose vaccinations than single dose and in vaccinated participants with previous infections. A negative correlation of IgG Positivity and level with age and time found in the study indicated monitoring of the seropositivity even after the booster dose administration might be required and elder population should be prioritized for vaccine administration.

5. Materials and method

Volunteers, with or without symptoms of SARS CoV-2 infection infection between March 2021 and April 2022 were enrolled in the study. A signed consent was obtained from each participant who was then asked to complete a questionnaire which contains participant's demographic information (age, gender, area of living, blood group etc.) and clinical information (presenting symptoms if any, history of co-morbidity etc.) Three ml blood was collected from each participant in a clot activator tube following standard protocol. After centrifuging the blood at 2000 rpm for 5 min the serum was separated and immediately stored at −20 °C if not processed the same day. All blood serum samples were tested within 72 h of collection.

Commercially available ELISA kit, Erbalisa COVID-19 IgG test kit, Erba Diagnostics Manheim Gmbh, Germany was used for the analysis of the blood sera. The test kit allows semi-quantitative detection of SARS CoV-2 IgG antibody in human serum. This European CE marked ELISA test kit has declared sensitivity and specificity of 98.3 and 98.1% respectively. Serum samples were tested by the ELISA kit as per the manufacturer's instruction [20]. In short, 10 μl serum samples were first diluted with commercially available sample diluent (1:200). 100 μl of the diluted samples were then dispensed in separate micro titer wells. The subsequent steps of incubation, washing, enzyme, substrate addition and stop solution were added as per manufacturer's guideline. The IgG index was

calculated according to instruction manual. IgG index of <0.9 was considered as negative whereas IgG index of ≥ 0.9 was considered as positive.

Participant's demographic characteristics were expressed as frequency and proportions. Normality of the data was checked with histogram with normal curve. IgG level were expressed as mean and shown with boxplot. Proportion test was applied to compare the IgG positivity among different groups and subgroups. Two sample t-tests were done to compare the mean of IgG index among various groups. Linear regression was applied to understand the IgG index with time in different age groups. STATA-13 was used for all the analysis.

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Ethical approval

The study was approved by the Research ethics committee of Bangladesh Reference Institute for Chemical Measurements (BRiCM), ref no: BRiCM2205, date- April 11, 2022. Written consent was taken from all the participants. Data were restricted to authorized person only and analyzed anonymously.

Author contribution statement

Mamudul Hasan Razu: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data.

Zabed Bin Ahmed: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

Md. Iqbal Hossain, Md. Raisul Islam Rabby and Fatema Akter: Performed the experiments.

Pranab Karmaker, Md. Robin Khan and Md. Moniruzzaman: Contributed reagents, materials, analysis tools; Wrote the paper.

Mala Khan: Conceived and designed the experiments; Wrote the paper.

Data availability statement

Data included in article/supp. material/referenced in article.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.heliyon.2023.e17767.

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