IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 23, Issue 2 Ser. 4 (February. 2024), PP 65-74
www.iosrjournals.org

Antibody Status After a Booster Dose of Vaccine Against SARS-CoV-2 Among the Healthcare Providers of Bangabandhu Sheikh Mujib Medical University(BSMMU)

Khaja Badruddza[1*], Mohammad Masum Alam[2], Sifat Naisum Rahman[3], Shahriar Habib[4], Farzana Islam[5], Md. Hanif Howlader[6], Forhadul Hoque Mollah[7]

[1*] *Department of Biochemistry, Sher-E-Bangla Medical College, Barishal, Bangladesh*
[2] *Department of Biochemistry & Molecular Biology, BSMMU, Dhaka, Bangladesh*
[3] *Department of Biochemistry, Sheikh Sayera Khatun Medical College, Gopalganj, Bangladesh*
[4] *Department of Microbiology, Sher-E-Bangla Medical College, Barishal, Bangladesh*
[5] *Laboratory Service Division, Sheikh Hasina National Institute of Burn & Plastic Surgery, Dhaka, Bangladesh*
[6] *Department of Biochemistry, Sher-E-Bangla Medical College, Barishal, Bangladesh*
[7] *Department of Biochemistry & Molecular Biology, BSMMU, Dhaka, Bangladesh*

Abstract:
Background: *COVID-19 was highly pathogenic, transmissible, and threatened human life. Antibodies produced after vaccination played a vital role in patients' survival-reducing morbidity and mortality. The study showed the response to vaccines among healthcare providers and revealed the picture of antibody status which can encourage people to receive the booster dose of vaccines. This study also showed the path of immunological protection through a booster dose of vaccination.*
Materials and Methods: *The study was a prospective observational study that was conducted in the Department of Biochemistry and Molecular Biology, BSMMU, Dhaka, Bangladesh, from 1st March 2022 to 28th February 2023. According to inclusion and exclusion criteria, a total of 73 study subjects were selected for this study by convenience purposive sampling technique from the different departments of BSMMU.*
Results: *Before taking the booster dose against SARS-CoV-2 the median Anti-RBD IgG of SARS-CoV-2 level was 3117.30 Au/mL and three weeks after taking the booster dose the median Anti-RBD IgG was 12174.20 Au/mL. The antibody level was increased about 4 times following the booster dose. Both homologous booster and heterologous booster showed similar immune responses regardless of the vaccine regimen. Hypertensive participants produced fewer antibodies, 7790.00 Au/mL following booster dose compared to normotensive participants, 14665.50 Au/mL. Diabetic participants also produced fewer antibodies, 7092.25 Au/mL following booster dose compared to nondiabetic participants, 12713.30 Au/mL. However, both hypertensive as well as diabetic participants produced robust antibodies following booster doses. Moderna vaccine produced significantly higher levels of IgG (5175.40 Au/mL) compared to AstraZeneca (2385.70 Au/mL) (Adjusted p-value 0.032 < 0.05) and Sinopharm (1828.15 Au/mL) (Adjusted p-value 0.009 < 0.05).*
Conclusion: *A booster dose of vaccine against SARS-CoV-2 produced robust antibodies in healthy participants as well as participants with co-morbidities like hypertension and diabetes mellitus.*
Keywords: *SARS-CoV-2, Anti-RBD IgG, COVID-19 Vaccine, Homologous and Heterologous Booster Dose.*

Date of Submission: 09-02-2024 Date of Acceptance: 19-02-2024

I. Introduction

The most effective strategy to combat COVID-19 was found to be the preventive strategy by appropriate vaccines that primed the immune system before the first encounter with SARS-CoV-2[1]. Mass vaccination was considered the primary strategy to curtail this pandemic[2] with the ultimate goal of achieving herd immunity by fulfilling nearly 75-90% vaccination coverage[3]. SARS-CoV-2 or Severe Acute Respiratory Syndrome Coronavirus 2 is an enveloped, positive-sense, single-stranded RNA virus with crown-like appearance and a genome that encodes 4 viral structural proteins: spike, envelope, membrane, and nucleocapsid[4], among them spike proteins help the virus to enter host cells by binding to the main virus receptor- angiotensin-converting enzyme 2 (ACE2), and thus a promising target for the development of mRNA vaccines[5–7]. Immunization against SARS-CoV-2 is believed to elicit a strong immune response against the virus's spike protein, specifically its receptor binding domain (RBD)[8].

Antibodies to SARS-CoV-2 played a critical role in suppressing COVID-19 pathogenesis by disrupting antigen (viral spike protein) binding to the ACE2 receptor on the cell, which is a crucial initial molecular event and was controlled by the affinity of these antibodies to the viral antigen[9]. In COVID-19 individuals, IgM could be found within a week of the onset of symptoms, reaches a peak within 2-3 weeks, and then declines[10]. In comparison to IgM, IgG levels began to rise rapidly a little bit later[10] and played a vital role in long-term immune memory[11]. So, a detectable level of IgG & IgM provides information about the serological conversion over the disease course, as the detection of IgM suggested a recent SARS-CoV-2 infection and the detection of IgG indicated previous SARS-CoV-2 exposure or a vaccinated status[10]. IgG had a good correlation with patient survival and helped to minimize SARS-CoV-2 infection persistence[12] and also with a lower risk of SARS-CoV-2 reinfection in the subsequent 6 months[13].

Most COVID-19 vaccines require two doses to stimulate an immune response and provide protection against symptomatic illness, nonetheless, the advent of SARS-CoV-2 variants with numerous mutations prompted questions about the two doses regimen's efficacy[14,15]. According to data acquired from vaccination in various countries, vaccine effectiveness had decreased over time and varies among developing virus strains[16]. The decline in circulating antibodies had generated concerns about the need for a booster dose of vaccine to strengthen protection against SARS-CoV-2 infection[17]. The booster dosage of vaccine could reverse the reduction in antibody levels that occurs after 2nd dose of vaccine, and the efficacy of three dose regimen was far superior to that of two doses[18].

Due to a delay in viral clearance, COVID-19 patients with diabetes mellitus and hypertension showed greater mortality and morbidity rates than those under metabolic control[19]. About 30% of COVID-19 patients brought to the hospital are hypertensive, and 12% are diabetic[20], hence, boosters against SARS-CoV-2 were also emphasized in them.

The protection gained by 2nd dose and a booster dose of vaccine was vital for guiding the vaccination plans, with a big influence on public health regulations to stop the pandemic. Implementing a successful vaccination program was crucial, as well as learning how long immunity against SARS-CoV-2 lasts in recipients of 2nd and booster doses of vaccine. So, this study aimed to encourage people to take the booster dose of vaccine and assess the antibody levels in vaccinated healthcare providers before and after a booster dose of vaccine. Also, to assess the antibody level generated following booster in the hypertensive and diabetic groups among the vaccinated healthcare providers.

II. Material And Methods

The study was a prospective observational study that was conducted in the Department of Biochemistry and Molecular Biology, BSMMU, Dhaka, Bangladesh, from 1st March 2022 to 28th February 2023. According to inclusion and exclusion criteria, a total of 73 study subjects were selected for this study by convenience purposive sampling technique from the different departments of BSMMU.

Study Design: Prospective observational study

Study Location: In the Department of Biochemistry and Molecular Biology, BSMMU, a tertiary hospital in Dhaka, Bangladesh.

Study Duration: 1st March 2022 to 28th February 2023.

Sample size: 73 Participants.

Procedure methodology:

After getting ethical clearance from the Institutional Review Board (IRB), BSMMU, by convenience purposive sampling a total of 73 study subjects were selected according to inclusion and exclusion criteria from the different departments of BSMMU. The purpose and procedure of the study were explained in detail and informed written consent was taken from each study subject. Age, sex, BP, BMI, and history were collected by using a data collection sheet. A blood sample was collected for the estimation of Anti-RBD IgG just before taking the booster dose. The serum was separated and preserved at -70^0 C. After three weeks, two blood samples were taken. One for serum Anti-RBD IgG and the other for RBS. Serum Anti-RBD IgG before and after taking the booster dose was measured on Alinity i by using SARS-CoV-2 IgG II Quant Reagent Kit 06S61(Abbott, Ireland) as directed by the manufacturer. RBS was also measured on Alinity c by using Alinity c Glucose Reagent Kit (Abbott Ireland) according to manufacturer instructions.

Statistical analysis:

The collected data were entered, cleaned, sorted, and then processed with the help of the Statistical Package for the Social Sciences (SPSS) software version 26.0. The results were expressed as mean ± SD (standard deviation) for normally distributed data, median and interquartile range (IQR) for skewed data, and frequency (%). Statistics were performed by using the Wilcoxon Signed Rank Test, Mann-Whitney U Test, Kruskal-Wallis Test, and Bonferroni pairwise test. The p-value < 0.05 was considered as statistically significant.

III. Result

A total of 73 study subjects were enrolled in this prospective observational study. Among them n= 58 were male and most of the study participants (n=50) were below 40 years of age with a mean age of 35.51 ± 7.96. Different types of vaccines against SARS-CoV-2 had been administered to the study subjects as 1st and 2nd doses of vaccine. Among them, AstraZeneca was 24.66% (n=18), Pfizer was 31.51% (n=23), Moderna was 23.29% (n=17), Sinopharm was 16.44% (n=12), and Sinovac was 4.11% (n=3). Among the different types of vaccines, Pfizer was administered to most of the study subjects. As the 1st and 2nd dose, the study subjects received the same vaccine, however, all the study subjects received only Pfizer as the booster dose implying that some of the study subjects had received mixed vaccine regimens. The findings have been presented in the subsequent pages.

Table no 1: Characteristics features of the participants.

Features	Male (n=58, 79.45%)	Female (n=15, 20.55%)	Total (N=73, 100%)	Mean ± SD
Age distribution (Years)				
< 40	39 (53.42%)	11 (15.07%)	50 (68.49%)	35.51 ± 7.96
≥ 40	19 (26.03%)	04 (5.48%)	23 (31.51%)	
Body Mass Index (BMI) (Kg/m^2)				
18.5 – 22.9 (Normal weight)	14 (19.18%)	01 (1.37%)	15 (20.55%)	26.14 ± 3.93
23.0 – 24.9 (Overweight)	14 (19.18%)	02 (2.74%)	16 (21.92%)	
≥ 25.0 (Obese)	30 (41.09%)	12 (16.44%)	42 (57.53%)	
Blood Pressure (BP)				
Normotensive	42 (57.53%)	13 (17.81%)	55 (75.34%)	-
Hypertensive	16 (21.92%)	02 (2.74%)	18 (24.66%)	
Blood Sugar				
Nondiabetic	48 (65.75%)	13 (17.81%)	61 (83.56%)	-
Diabetic	10 (13.70%)	02 (2.74%)	12 (16.44%)	

Table no 1 shows the frequency (n) with percentage (%) of categorical variables and mean ± SD of continuous variables.

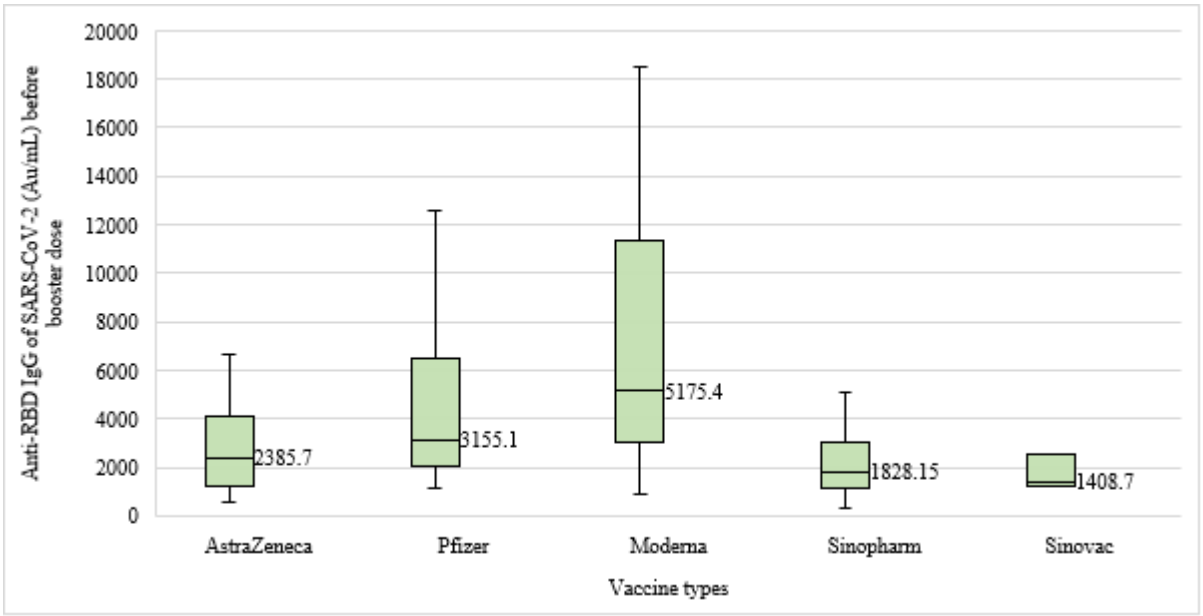

Figure no 1: Box-Whisker plot showing the comparison of Anti-RBD IgG of SARS-CoV-2 among the different types of vaccine before booster dose.

Table no 2: Comparison of anti-RBD IgG of SARS-CoV-2 among different types of vaccines before booster.

Anti-RBD IgG of SARS-CoV-2 elicited by different types of vaccine (Au/mL) Median (IQR)	**AstraZeneca n=18**	**Pfizer n=23**	**Moderna n=17**	**Sinopharm n=12**	**Sinovac n=3**	**p-value**
	2385.70 (1218.3 - 4122.5)	**3155.10** (2029.3 - 6475.6)	**5175.40** (3375.2 - 10858.3)	**1828.15** (1155.35 - 2878.7)	**1408.70** (1194.5 - 2575.5)	**0.002**

Table no 2 shows the comparison of Anti-RBD IgG of SARS-CoV-2 elicited by different types of vaccines that were administered to immunize the study subjects. Kruskal-Wallis Test was done as a test of significance to analyze the data which revealed a significant difference in antibody levels among different types of vaccine (p-value < 0.05).

Table no 3: Pairwise comparison of Anti-RBD IgG of SARS-CoV-2 among the different types of vaccines.

	Sample 1 – Sample 2	**p-value**	**Adjusted p-value (p-value*Number of test)**
1	Sinovac – Sinopharm	0.766	1.000
2	Sinovac – AstraZeneca	0.473	1.000
3	Sinovac – Pfizer	0.079	0.799
4	**Sinovac – Moderna**	**0.021**	0.212
5	Sinopharm – AstraZeneca	0.493	1.000
6	**Sinopharm – Pfizer**	**0.013**	0.132
7	**Sinopharm – Moderna**	**0.001**	**0.009**
8	**AstraZeneca – Pfizer**	**0.046**	0.462
9	**AstraZeneca – Moderna**	**0.003**	**0.032**
10	Pfizer – Moderna	0.249	1.000

Table no 3 shows the pairwise comparison of Anti-RBD IgG of SARS-CoV-2 among the different types of vaccines. There is a significant difference in IgG levels among the different types of vaccines. Post hoc analysis with the Bonferroni method revealed that Moderna vaccine produced significantly higher levels of IgG compared to AstraZeneca and Sinopharm.

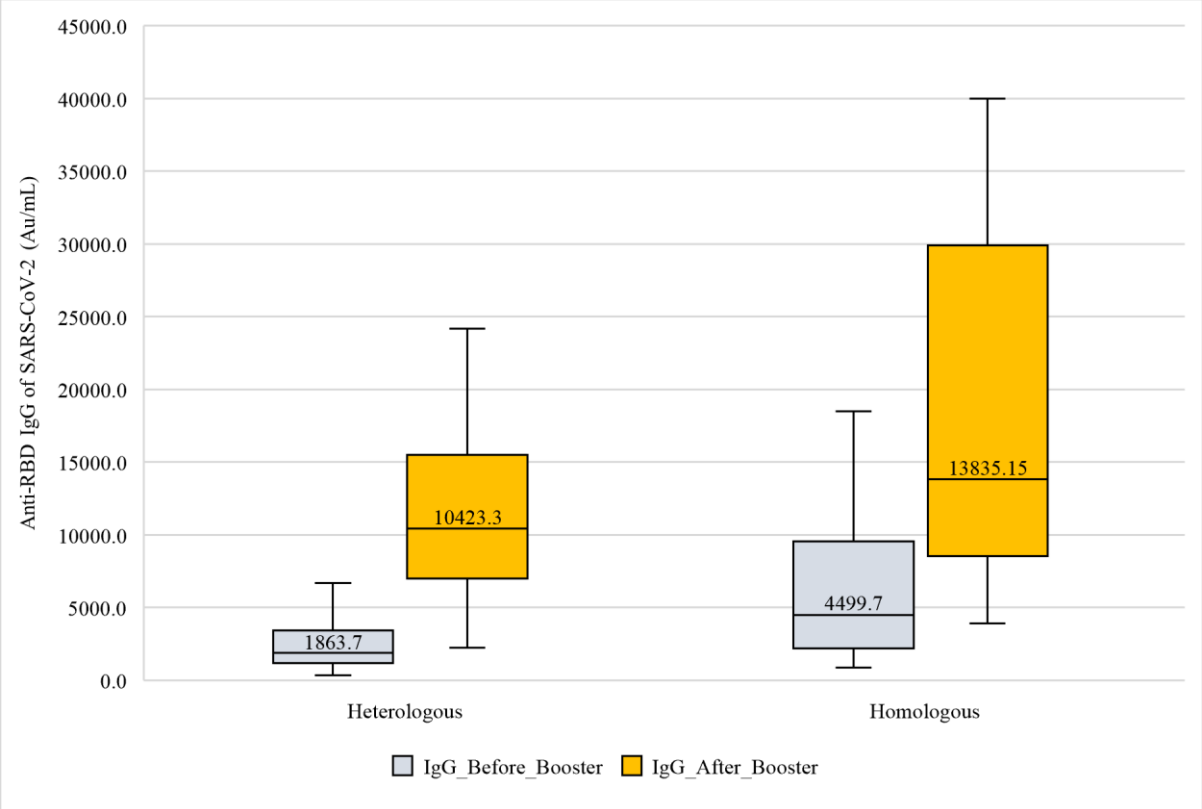

Figure no 2: Box and whisker plot showing the median antibody levels between vaccine regimens before and after the booster dose of vaccine against SARS-CoV-2.

Table no 4: Comparison of Anti-RBD IgG of SARS-CoV-2 level before and after three weeks of a booster dose of COVID-19 vaccine.

IgG of SARA-Cov-2 / Study subjects	Anti-RBD IgG of SARS-CoV-2 before taking a booster dose of vaccine (Au/mL) Median (IQR)	Anti-RBD IgG of SARS-CoV-2 three weeks after taking a booster dose of vaccine (Au/mL) Median (IQR)	p-value
Total (N = 73)	3117.30 (1527.70 – 5026.00)	12174.20 (7576.60 – 19840.95)	<0.001
Vaccine regimen			
Homologous booster (n = 40)	4499.70 (2202.20– 9013.90)	13835.15 (8804.45– 28881.05)	< 0.001
Heterologous booster (n = 33)	1863.70 (1194.50– 3196.80)	10423.30 (7325.30– 15123.20)	< 0.001

Table 4 shows the comparison of Anti-RBD IgG of SARS-CoV-2 level before taking the booster dose and three weeks after taking the booster dose among the study subjects. Wilcoxon Signed Rank Test was done to analyze the data which revealed a significantly higher antibody level in three weeks after taking the booster dose of vaccine compared to before taking the booster dose of vaccine (p-value < 0.001).

Table no 5: Comparison of Anti-RBD IgG of SARS-CoV-2 level before and after three weeks of a booster dose of COVID-19 vaccine between homologous booster and heterologous booster vaccine regimen.

Vaccine regimen / IgG of SARA-Cov-2	Homologous booster (n = 40)	Heterologous booster (n = 33)	p-value
Anti-RBD IgG of SARS-CoV-2 before taking a booster dose of vaccine (Au/mL) Median (IQR)	4499.70 (2202.20– 9013.90)	1863.70 (1194.50– 3196.80)	< 0.001
Anti-RBD IgG of SARS-CoV-2 three weeks after taking a booster dose of vaccine (Au/mL) Median (IQR)	13835.15 (8804.45– 28881.05)	10423.30 (7325.30– 15123.20)	0.013

Table no 5 shows the comparison of Anti-RBD IgG of SARS-CoV-2 level before taking the booster dose between homologous booster and heterologous booster vaccine regimen and the comparison of Anti-RBD IgG of SARS-CoV-2 level three weeks after taking the booster dose between homologous booster and heterologous booster vaccine regimen. Mann-Whitney U Test was done to analyze the data which revealed a significant difference in antibody levels between homologous booster and heterologous booster vaccine regimen before taking the booster dose (p-value < 0.001) and also three weeks after taking the booster dose of vaccine (p-value 0.013 <0.05).

Table no 6: Comparison of Anti-RBD IgG of SARS-CoV-2 level before and after three weeks of a booster dose of COVID-19 vaccine between normotensive and hypertensive groups of the study subjects.

Blood Pressure / IgG of SARA-Cov-2	Normotensive (n = 55)	Hypertensive (n = 18)	p-value
Anti-RBD IgG of SARS-CoV-2 before taking a booster dose of vaccine (Au/mL) Median (IQR)	3196.80 (1676.40 – 5414.90)	1946.50 (1194.50 – 3486.70)	0.046
Anti-RBD IgG of SARS-CoV-2 three weeks after taking a booster dose of vaccine (Au/mL) Median (IQR)	14665.50 (8849.00 – 24181.10)	7790.00 (3690.40 – 12174.20)	< 0.001

Table no 6 shows the comparison of Anti-RBD IgG of SARS-CoV-2 level before taking the booster dose between normotensive and hypertensive study subjects and the comparison of Anti-RBD IgG of SARS-CoV-2 level three weeks after taking the booster dose between normotensive and hypertensive study subjects. Mann-Whitney U Test was done to analyze the data which revealed a significant difference in antibody levels between normotensive and hypertensive study subjects before taking the booster dose (p-value 0.046 < 0.05) and also three weeks after taking the booster dose of vaccine (p-value <0.001).

Table no 7: Comparison of Anti-RBD IgG of SARS-CoV-2 level before and after three weeks of a booster dose of COVID-19 vaccine between nondiabetic and diabetic groups of the study subjects.

Diabetes Mellitus / IgG of SARA-CoV-2	Nondiabetic (n = 61)	Diabetic (n = 12)	p-value
Anti-RBD IgG of SARS-CoV-2 before taking a booster dose of vaccine (Au/mL) Median (IQR)	3155.10 (1792.60 – 5175.40)	1592.55 (1041.30 – 3554.20)	0.048
Anti-RBD IgG of SARS-CoV-2 three weeks after taking a booster dose of vaccine (Au/mL) Median (IQR)	12713.30 (8849.00 – 21120.60)	7092.25 (4403.90 – 11607.80)	0.003

Table no 7 shows the comparison of Anti-RBD IgG of SARS-CoV-2 level before taking the booster dose between nondiabetic and diabetic study subjects and the comparison of Anti-RBD IgG of SARS-CoV-2 level three weeks after taking the booster dose between nondiabetic and diabetic study subjects. Mann-Whitney U Test was done to analyze the data which revealed a significant difference in antibody levels between nondiabetic and diabetic study subjects before taking the booster dose (p-value 0.048 < 0.05) and also three weeks after taking the booster dose of vaccine (p-value 0.003 <0.05).

IV. Discussion

The invention of the vaccine has given humanity new hope in the fight against the highly contagious COVID-19 as well as mass vaccination is seen to be the most effective way to stop this epidemic. The regulatory authorities have approved several vaccines. The outcomes of the widespread immunization efforts indicate that using the recommended vaccine doses has significantly increased the protection against COVID-19 and has been linked to a significant decline in COVID-19-related hospitalizations and fatalities. The human body produces both IgM and IgG antibodies in response to a vaccine. This prospective observational study aimed to measure and compare the levels of antibodies (IgG) directed against the spike protein of SARS-CoV-2 before and after a booster dose of vaccine. The 1st blood sample was taken at least 4 months after 2nd dose of vaccine, and 2nd blood sample was taken three weeks after the 3rd dose, i.e., booster dose of vaccine. Therefore, it was worth trying to find out the levels and comparison of antibodies before and after a booster dose of vaccine against SARS-CoV-2. Participants were enrolled based on inclusion and exclusion criteria.

Effect of different types of vaccines on Anti-RBD IgG levels before receiving a booster dose of the COVID-19 vaccine:

Different types of vaccines against SARS-CoV-2 had been administered to the study subjects as 1st and 2nd doses of vaccine. Among the different types of vaccines, Pfizer was administered to most of the study subjects (31.51%, n=23), followed by AstraZeneca (24.66%, n=18), Moderna (23.29%, n=17), Sinopharm (16.44%, n=12), and Sinovac (4.11%, n=3). This study showed that participants who were vaccinated with Moderna produced maximum IgG against SARS-CoV-2 compared to others who were vaccinated with other than Moderna (Figure no 1). The median antibody levels for different vaccines were AstraZeneca 2385.70 Au/mL, Pfizer 3155.10 Au/mL, Moderna 5175.40 Au/mL, Sinopharm 1828.15 Au/mL, and Sinovac 1408.70 Au/mL (Table no 2). Kruskal-Walis Test was done as a test of significance and the p-value was found 0.002 which was < 0.05 and statistically significant. Post hoc analysis with the Bonferroni method revealed that Moderna vaccine produced significantly higher levels of IgG compared to AstraZeneca and Sinopharm (Table no 3). Similarly, another research was conducted by Sarker et al. in Bangladesh and found that Moderna and Pfizer produced significantly higher antibody titers compared to the AstraZeneca and Sinopharm vaccines[21]. Another study done by Steensels et al. demonstrated that Moderna elicited more antibodies compared to Pfizer both in uninfected as well as infected participants[22].

Anti-RBD IgG levels before and after receiving a booster dose of the COVID-19 vaccine:

Anti-RBD IgG of SARS-CoV-2 levels before taking the booster dose and three weeks after taking the booster dose was analyzed and found median antibody levels three weeks after taking the booster dose were higher (12174.20 Au/mL) compared to before taking the booster dose (3117.30 Au/mL) (Table no 4). Wilcoxon Signed Rank Test was done as a test of significance and the p-value was found < 0.001 which was statistically significant. It was found that three weeks after taking the booster dose antibodies levels increased about 4 times compared to before taking the booster dose. A longitudinal study was done by Tanaka et al. on healthcare workers at Izumi City General Hospital, Osaka, Japan, and found that after the 3rd dosage, the peak anti-spike IgG titer was roughly 4.1 times higher than it was after the 2nd dose[23]. A similar study done by Eliakim–Raz et al showed that a 3rd dose of vaccine in adults aged ≥ 60 years was associated with significantly increased levels of IgG[24]. Similarly, Gilboa

et al. showed a quick and extensive immune response to 3rd dose of vaccine, as evidenced by a considerable rise in IgG levels[25]. It's noteworthy that both researches involved healthy adults older than 60 years. Another study on French nursing home residents done by Blain et al. showed a rapid decay of RBD-IgG levels after the 2nd vaccine dose and a significant increase after the 3rd vaccine dose administration[26]. Cucunawangsih et al. showed that 3rd dose of vaccine elicited a strong antibody response against SARS-CoV-2 in 90 healthcare providers from Siloam Teaching Hospital, Indonesia, with a median age of 31 years[27].

Effect of homologous booster and heterologous booster regimen on Anti-RBD IgG levels:

All the study subjects received the same types of vaccine as the 1st and 2nd doses of vaccine schedules. However, only Pfizer was administered to all the study subjects as the booster dose of the vaccine. Hence, the study group was further divided into homologous booster (n=40) and heterologous booster groups depending on whether they received the same type (i.e., mRNA) of vaccine in all three doses or not. The booster was considered a homologous booster when the platform was similar to the primarily administered vaccine, i.e., 1st and 2nd dose, and heterologous booster when the platform was different. As mentioned earlier, the median Anti-RBD IgG level for all 73 study subjects before taking a booster dose of the SARS-CoV-2 vaccine was 3117.30 Au/mL. Three weeks after receiving the booster dose, the median Anti-RBD IgG level significantly increased to 12174.20 Au/mL (with a p-value of <0.001). This substantial increase in IgG levels suggests a robust immune response following the booster dose. To make a comparison by vaccine regimen, the median Anti-RBD IgG level before the booster and three weeks after the booster were 4499.70 Au/mL and 13835.15 Au/mL respectively in the case of homologous booster group (n = 40) showing a significant boost in IgG levels; while in the heterologous booster group (n = 33), the median Anti-RBD IgG level before the booster and three weeks after the booster was 1863.70 Au/mL and 10423.30 Au/mL, also showing a similar substantial increase in IgG levels (Table no 4). The homologous booster group had higher IgG levels both before and after the booster compared to the heterologous booster group (Figure no 2). The p-value for the change in IgG levels before the booster was <0.001 for both groups and the p-value for the post-booster IgG levels between the two groups was also significant (0.013) (Table no 5). Although the heterologous booster group showed a higher fold rise of titer (about 5-fold) than the homologous booster group (about 3-fold), this suggests that the booster effect was similar regardless of the vaccine regimen. In summary, both homologous and heterologous booster regimens significantly enhanced anti-RBD IgG levels, emphasizing the importance of booster doses in maintaining strong immune responses against SARS-CoV-2. Similar findings were also observed by Atmar et al., Orlandi et al., and González et al. showing robust booster effects that were similar regardless of the vaccine regimen[28–30].

Effect of hypertensive status on Anti-RBD IgG levels after receiving a booster dose of the COVID-19 vaccine:

Before taking the booster dose the median antibodies in normotensive study subjects (n=55) were 3196.80 Au/mL and that of hypertensive subjects were 1946.50 Au/mL (Table no 6). Normotensive study subjects had higher median antibody levels than hypertensive study subjects and the difference was statistically significant (p-value 0.046 < 0.05). Three weeks after taking the booster dose the median antibodies in normotensive study subjects were 14665.50 Au/mL and that of hypertensive subjects were 7790.00 Au/mL. In this case, normotensive study subjects had also higher median antibody levels than hypertensive study subjects and the difference was statistically significant (p-value < 0.001). In summary, both normotensive and hypertensive individuals in this study exhibit increased Anti-RBD IgG levels after receiving a booster dose of the COVID-19 vaccine, with a more pronounced effect observed in the normotensive group. In a study in Rome, Italy, Watanabe et al. observed a similar result in which a hypertensive individual, following the SARS-CoV-2 mRNA vaccine, elicited less antibody[31]. Another study was done by Soegiarto et al. in Indonesia and the most important findings of their study were the association between hypertension and lower antibody response following SARS-CoV-2 vaccination[32]. Recent data shows that the immune system may be related to hypertension. A major alteration in T cell immune metabolism can lead to abnormal T cell activation, differentiation, and proliferation and ultimately lead to the development of hypertension[33,34]. Hypertensive individuals displayed lower lymphocyte count compared to a normotensive individual; As lymphocytes are crucial in the immune response to vaccination, this finding may reveal a connection between hypertension and the successful treatment of hypertension may not affect the immune response to vaccination[32].

Effect of diabetic status on Anti-RBD IgG levels after receiving a booster dose of the COVID-19 vaccine:

In this study, 83.56% (n=61) of the total study subjects were nondiabetic and the median antibodies before taking the booster dose in those study subjects were 3155.10 Au/mL, while that of diabetic subjects were 1592.55 Au/mL. Diabetic study subjects had lower antibody levels than nondiabetic study subjects and were statistically significant (p-value 0.048 < 0.05). Three weeks after taking the booster dose the median antibodies in nondiabetic subjects were 12713.30 Au/mL and that of diabetic subjects were 7092.25 Au/mL. In this case,

diabetic study subjects had also lower antibody levels than nondiabetic study subjects and were statistically significant (p-value 0.003 < 0.05). In summary, in this study, both nondiabetic and diabetic individuals exhibit increased anti-RBD IgG levels after receiving a booster dose of the COVID-19 vaccine. However, the magnitude of this increase appears to be more pronounced in the nondiabetic group. A study done by Ali et al. showed that after receiving the BNT162b2 mRNA COVID-19 vaccine, both diabetic and non-diabetic individuals had high antibody levels but the diabetic individual had significantly lower antibody levels than nondiabetic individual[35]. Similar findings were found by Habib et al. showing that diabetic individuals with poor glycemic control had a lower immune response than nondiabetic individual[36]. Another study done by Soetedjo et al. demonstrated that following vaccination against SARS-CoV-2 diabetic patients had lower antibody levels compared to healthy controls but the antibody response in diabetic patients was still robust[37]. With COVID-19, patients with DM are more likely to have a poor prognosis, which is partially explained by the immunological dysfunction prevalent in DM[38]. Patients with DM had impaired function of both the innate and adaptive components of the immune system[39]. T-helper cell signals are necessary for B-lymphocytes to activate plasma cells that produce antibodies; People with DM may have improperly differentiated T-helper cells[40]. So, priority should be given to all diabetic patients to have the immunization against SARS-CoV-2 on schedule.

V. Conclusion

It was observed in this study that a booster dose of vaccine against SARS-CoV-2 significantly increased the antibody levels. Hypertensive & diabetic individuals had lower antibody levels in response to a vaccine. It was also observed that Moderna was more effective than AstraZeneca and Sinopharm vaccines. Taken together, the relevance of the booster dosage was supported by research in both healthy and susceptible individuals. From a serological point of view, the efficacy of the booster dose should be consolidated by a clinical point of view.

Limitations

a) Relatively small sample size, making it difficult to assess subgroup effects.
b) The study was conducted on the healthcare providers in a single center, so it was not representative of the whole population.
c) The study did not measure peak antibody levels following 1st & 2nd doses of vaccines, which would have made its conclusion more acceptable.
d) The study could not measure the immune responses in other varieties of heterologous booster regimens (e.g., killed vaccine, vector vaccine) other than mRNA vaccines.

Recommendations

a) It is necessary to carry out a multicenter study throughout the country with a large sample size throughout the general population.
b) Further study should be conducted based on the durability of the antibody that was produced following the booster dose. It will provide important information on whether a further booster dose will be needed or not.

Conflict of interest

The authors declare that the research was carried out without any financial or commercial ties that may be seen as having a conflict of interest.

Ethical Statement

This study was reviewed and approved by the IRB of BSMMU (reference: BSMMU/2022/7268, registration number: 3986, date: 27-07-2022). Participants were assured about their confidentiality and were free to withdraw from the study at any time.

Acknowledgments

This study was funded by a research grant from BSMMU, Dhaka, Bangladesh.

Author contributions

All authors participated in the article and authorized the submitted version.

Data availability

The authors will provide the raw data used to support the results of this study upon request.

References

[1] Achiron A, Mandel M, Dreyer-Alster S, Harari G, Gurevich M. Humoral Sars-Cov-2 Igg Decay Within 6 Months In Covid-19 Healthy Vaccinees: The Need For A Booster Vaccine Dose? Eur J Intern Med. 2021;94:105-107. Doi:10.1016/J.Ejim.2021.10.027

[2] Yelin I, Katz R, Herzel E, Berman-Zilberstein T, Ben-Tov A, Kuint J, Et Al. Associations Of The Bnt162b2 Covid-19 Vaccine Effectiveness With Patient Age And Comorbidities. Doi:10.1101/2021.03.16.21253686

[3] Anderson Rm, Vegvari C, Truscott J, Collyer Bs. Challenges In Creating Herd Immunity To Sars-Cov-2 Infection By Mass Vaccination. The Lancet. 2020;396(10263):1614-1616. Doi:10.1016/S0140-6736(20)32318-7

[4] Nomura Y, Sawahata M, Nakamura Y, Kurihara M, Koike R, Katsube O, Et Al. Age And Smoking Predict Antibody Titres At 3 Months After The Second Dose Of The Bnt162b2 Covid-19 Vaccine. Vaccines (Basel). 2021;9(9). Doi:10.3390/Vaccines9091042

[5] Song Z, Xu Y, Bao L, Zhang L, Yu P, Qu Y, Et Al. From Sars To Mers, Thrusting Coronaviruses Into The Spotlight. Viruses. 2019;11(1). Doi:10.3390/V11010059

[6] Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, Et Al. Sars-Cov-2 Cell Entry Depends On Ace2 And Tmprss2 And Is Blocked By A Clinically Proven Protease Inhibitor. Cell. 2020;181(2):271-280.E8. Doi:10.1016/J.Cell.2020.02.052

[7] Jiang S, Lu L, Liu Q, Xu W, Du L. Receptor-Binding Domains Of Spike Proteins Of Emerging Or Re-Emerging Viruses As Targets For Development Of Antiviral Vaccines. Emerg Microbes Infect. 2012;1. Doi:10.1038/Emi.2012.1

[8] Barnes Co, Jette Ca, Abernathy Me, Dam Kma, Esswein Sr, Gristick Hb, Et Al. Sars-Cov-2 Neutralizing Antibody Structures Inform Therapeutic Strategies. Nature. 2020;588(7839):682-687. Doi:10.1038/S41586-020-2852-1

[9] Fiedler S, Piziorska Ma, Denninger V, Morgunov As, Ilsley A, Malik Ay, Et Al. Antibody Affinity Governs The Inhibition Of Sars-Cov-2 Spike/Ace2 Binding In Patient Serum. Acs Infect Dis. 2021;7(8):2362-2369. Doi:10.1021/Acsinfecdis.1c00047

[10] Hou H, Wang T, Zhang B, Luo Y, Mao L, Wang F, Et Al. Detection Of Igm And Igg Antibodies In Patients With Coronavirus Disease 2019. Clin Transl Immunology. 2020;9(5). Doi:10.1002/Cti2.1136

[11] Racine R, Winslow Gm. Igm In Microbial Infections: Taken For Granted? Immunol Lett. 2009;125(2):79-85. Doi:10.1016/J.Imlet.2009.06.003

[12] Dispinseri S, Secchi M, Pirillo Mf, Tolazzi M, Borghi M, Brigatti C, Et Al. Neutralizing Antibody Responses To Sars-Cov-2 In Symptomatic Covid-19 Is Persistent And Critical For Survival. Nat Commun. 2021;12(1). Doi:10.1038/S41467-021-22958-8

[13] Lumley Sf, O'donnell D, Stoesser Ne, Matthews Pc, Howarth A, Hatch Sb, Et Al. Antibody Status And Incidence Of Sars-Cov-2 Infection In Health Care Workers. New England Journal Of Medicine. 2021;384(6):533-540. Doi:10.1056/Nejmoa2034545

[14] Madhi Sa, Baillie V, Cutland Cl, Voysey M, Koen Al, Fairlie L, Et Al. Efficacy Of The Chadox1 Ncov-19 Covid-19 Vaccine Against The B.1.351 Variant. New England Journal Of Medicine. 2021;384(20):1885-1898. Doi:10.1056/Nejmoa2102214

[15] Zhang Y, Zeng G, Pan H, Li C, Hu Y, Chu K, Et Al. Safety, Tolerability, And Immunogenicity Of An Inactivated Sars-Cov-2 Vaccine In Healthy Adults Aged 18–59 Years: A Randomised, Double-Blind, Placebo-Controlled, Phase 1/2 Clinical Trial. Lancet Infect Dis. 2021;21(2):181-192. Doi:10.1016/S1473-3099(20)30843-4

[16] Wu N, Joyal-Desmarais K, Ribeiro Pab, Vieira Am, Stojanovic J, Sanuade C, Et Al. Long-Term Effectiveness Of Covid-19 Vaccines Against Infections, Hospitalisations, And Mortality In Adults: Findings From A Rapid Living Systematic Evidence Synthesis And Meta-Analysis Up To December, 2022. Lancet Respir Med. 2023;11(5):439-452. Doi:10.1016/S2213-2600(23)00015-2

[17] Lo Sasso B, Agnello L, Giglio Rv, Gambino Cm, Ciaccio Am, Vidali M, Et Al. Longitudinal Analysis Of Anti-Sars-Cov-2 S-Rbd Igg Antibodies Before And After The Third Dose Of The Bnt162b2 Vaccine. Sci Rep. 2022;12(1):8679. Doi:10.1038/S41598-022-12750-Z

[18] Yue L, Xie T, Yang T, Zhou J, Chen H, Zhu H, Et Al. A Third Booster Dose May Be Necessary To Mitigate Neutralizing Antibody Fading After Inoculation With Two Doses Of An Inactivated Sars-Cov-2 Vaccine. J Med Virol. 2022;94(1):35-38. Doi:10.1002/Jmv.27334

[19] Abu-Farha M, Al-Mulla F, Thanaraj Ta, Kavalakatt S, Ali H, Abdul Ghani M, Et Al. Impact Of Diabetes In Patients Diagnosed With Covid-19. Front Immunol. 2020;11. Doi:10.3389/Fimmu.2020.576818

[20] Fang L, Karakiulakis G, Roth M. Are Patients With Hypertension And Diabetes Mellitus At Increased Risk For Covid-19 Infection? Lancet Respir Med. 2020;8(4):E21. Doi:10.1016/S2213-2600(20)30116-8

[21] Sarker P, Akhtar E, Kuddusi Ru, Alam Mm, Haq Ma, Hosen Mb, Et Al. Comparison Of The Immune Responses To Covid-19 Vaccines In Bangladeshi Population. Vaccines (Basel). 2022;10(9). Doi:10.3390/Vaccines10091498

[22] Steensels D, Pierlet N, Penders J, Mesotten D, Heylen L. Comparison Of Sars-Cov-2 Antibody Response Following Vaccination With Bnt162b2 And Mrna-1273. Jama. 2021;326(15):1533. Doi:10.1001/Jama.2021.15125

[23] Tanaka H, Mukai J, Kushibiki K, Mizushima S, Maeda K, Fujimoto Y, Et Al. Effect Of The Third Dose Of Bnt162b2 Covid-19 Mrna Vaccine On Anti-Sars-Cov-2 Antibody Levels In Healthcare Workers. Vaccine. Published Online January 9, 2022. Doi:10.1016/J.Vaccine.2022.11.049

[24] Eliakim-Raz N, Leibovici-Weisman Y, Stemmer A, Ness A, Awwad M, Ghantous N, Et Al. Antibody Titers Before And After A Third Dose Of The Sars-Cov-2 Bnt162b2 Vaccine In Adults Aged ≥60 Years. Jama. 2021;326(21):2203. Doi:10.1001/Jama.2021.19885

[25] Gilboa M, Mandelboim M, Indenbaum V, Lustig Y, Cohen C, Rahav G, Et Al. Early Immunogenicity And Safety Of The Third Dose Of Bnt162b2 Messenger Rna Coronavirus Disease 2019 Vaccine Among Adults Older Than 60 Years: Real-World Experience. Journal Of Infectious Diseases. 2022;225(5):785-792. Doi:10.1093/Infdis/Jiab584

[26] Blain H, Tuaillon E, Gamon L, Pisoni A, Miot S, Picot Mc. Strong Decay Of Sars-Cov-2 Spike Antibodies After 2 Bnt162b2 Vaccine Doses And High Antibody Response To A Third Dose In Nursing Home Residents. J Am Med Dir Assoc. 2022;23(5):750-753. Doi:10.1016/J.Jamda.2022.02.006

[27] Cucunawangsih C, Wijaya Rs, Lugito Nph, Suriapranata I. Antibody Response After A Third Dose Mrna-1273 Vaccine Among Vaccinated Healthcare Workers With Two Doses Of Inactivated Sars-Cov-2 Vaccine. International Journal Of Infectious Diseases. 2022;118:116-118. Doi:10.1016/J.Ijid.2022.02.036

[28] Atmar Rl, Lyke Ke, Deming Me, Jackson La, Branche Ar, El Sahly Hm, Et Al. Homologous And Heterologous Covid-19 Booster Vaccinations. New England Journal Of Medicine. 2022;386(11):1046-1057. Doi:10.1056/Nejmoa2116414

[29] Orlandi C, Stefanetti G, Barocci S, Buffi G, Diotallevi A, Rocchi E, Et Al. Comparing Heterologous And Homologous Covid-19 Vaccination: A Longitudinal Study Of Antibody Decay. Viruses. 2023;15(5). Doi:10.3390/V15051162

[30] González S, Olszevicki S, Gaiano A, Salazar M, Regairaz L, Varela Baino An, Et Al. Protection Of Homologous And Heterologous Boosters After Primary Schemes Of Rad26-Rad5, Chadox1 Ncov-19 And Bbibp-Corv During The Omicron Outbreak In Adults Of 50 Years And Older In Argentina: A Test-Negative Case–Control Study. Lancet Regional Health - Americas. 2023;27. Doi:10.1016/J.Lana.2023.100607

[31] Watanabe M, Balena A, Tuccinardi D, Tozzi R, Risi R, Masi D, Et Al. Central Obesity, Smoking Habit, And Hypertension Are Associated With Lower Antibody Titres In Response To Covid-19 Mrna Vaccine. Diabetes Metab Res Rev. 2022;38(1). Doi:10.1002/Dmrr.3465

[32] Soegiarto G, Wulandari L, Purnomosari D, Dhia Fahmita K, Ikhwan Gautama H, Tri Hadmoko S, Et Al. Hypertension Is Associated With Antibody Response And Breakthrough Infection In Health Care Workers Following Vaccination With Inactivated Sars-Cov-2. Vaccine. 2022;40(30):4046-4056. Doi:10.1016/J.Vaccine.2022.05.059

[33] Moshfegh Cm, Case Aj. The Redox-Metabolic Couple Of T Lymphocytes: Potential Consequences For Hypertension. Antioxid Redox Signal. 2021;34(12):915-935. Doi:10.1089/Ars.2020.8042

[34] Rai A, Narisawa M, Li P, Piao L, Li Y, Yang G, Et Al. Adaptive Immune Disorders In Hypertension And Heart Failure: Focusing On T-Cell Subset Activation And Clinical Implications. J Hypertens. 2020;38(10):1878-1889. Doi:10.1097/Hjh.0000000000002456
[35] Ali H, Alterki A, Sindhu S, Alahmad B, Hammad M, Al-Sabah S, Et Al. Robust Antibody Levels In Both Diabetic And Non-Diabetic Individuals After Bnt162b2 Mrna Covid-19 Vaccination. Front Immunol. 2021;12. Doi:10.3389/Fimmu.2021.752233
[36] Habib S, Nessa A, Islam F, Akther T. Immune Responses To Bnt162b2 Sars-Cov-2 Mrna Vaccine In T2dm Individuals In Bangladesh. Iosr Journal Of Dental And Medical Sciences (Iosr-Jdms) E-Issn. 2023;22:39-47. Doi:10.9790/0853-2212023947
[37] Soetedjo Nnm, Iryaningrum Mr, Lawrensia S, Permana H. Antibody Response Following Sars-Cov-2 Vaccination Among Patients With Type 2 Diabetes Mellitus: A Systematic Review. Diabetes And Metabolic Syndrome: Clinical Research And Reviews. 2022;16(2). Doi:10.1016/J.Dsx.2022.102406
[38] Pal R, Bhansali A. Covid-19, Diabetes Mellitus And Ace2: The Conundrum. Diabetes Res Clin Pract. 2020;162. Doi:10.1016/J.Diabres.2020.108132
[39] Pal R, Sachdeva N, Mukherjee S, Suri V, Zohmangaihi D, Ram S, Et Al. Impaired Anti-Sars-Cov-2 Antibody Response In Non-Severe Covid-19 Patients With Diabetes Mellitus: A Preliminary Report. Diabetes And Metabolic Syndrome: Clinical Research And Reviews. 2021;15(1):193-196. Doi:10.1016/J.Dsx.2020.12.035
[40] Erener S. Diabetes, Infection Risk And Covid-19. Mol Metab. 2020;39. Doi:10.1016/J.Molmet.2020.101044