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Evaluation of SARS-CoV-2 antibody decay over time following booster dose administration: A prospective observational study

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Abstract
Background: Evaluating the decay of SARS-CoV-2 antibodies over time following a booster dose is critical for understanding the longevity and efficacy of COVID-19 immunity. The rate at which antibodies decrease post-booster can vary based on factors like vaccine type, individual health, and age. This study aimed to assess the temporal decay of SARS-CoV-2 antibodies after booster dose administration.
Methods: This prospective observational study was carried out at the Department of Biochemistry & Molecular Biology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, from March 2022 to February 2023. The study included 80 adult participants aged 25 to 65, who received their COVID-19 booster dose approximately 6–8 months prior. Participants were selected using purposive sampling. Data analysis was performed using SPSS version 26.0.
Results: The study found a significant decrease in serum IgG levels at 3 month's interval who had taken booster dose 6-8 months ago, with p-values indicating strong statistical significance ($p<0.001$). This decline was consistently observed ($p<0.05$) across various groups, including different genders, infection, and vaccination statuses, age ranges (25-44 and 45-65), all BMI categories, and individuals with comorbidities such as diabetes (DM) and hypertension (HTN). Although all booster types showed a decrease in IgG levels, the decline was not significant for the Moderna vaccine ($p>0.05$), whereas significant reductions were noted for the other boosters ($p<0.05$).
Conclusion: After a booster dose, antibody levels, particularly serum IgG significantly declined at three months interval who had taken booster dose six to eight months earlier, irrespective of age, gender, infection status, vaccination status, BMI, diabetes, and hypertension. All booster types showed reduced IgG levels, but the decline with Moderna was insignificant, indicating variability by vaccine type.

Keywords: antibodies, adult, booster dose, decaying, sars-cov-2, serum igg

Introduction
The COVID-19 pandemic drove significant vaccine development, successfully controlling SARS-CoV-2 spread [1]. Post-vaccine rollout, a key question is the duration of immunity, especially after booster doses [2]. Understanding antibody decay is essential for shaping public health strategies and vaccination policies for current and future outbreaks [3]. Initial studies showed that the primary COVID-19 vaccine series elicited strong immune responses with neutralizing antibodies and cellular immunity [4]. However, antibody levels began to wane within months after the primary vaccination series [5], raising concerns about a potential drop in vaccine efficacy, particularly against new variants with immune evasion [1]. To combat this, booster doses were introduced to boost immunity, resulting in rapid antibody increases and better protection against severe disease [6]. While initial data indicate these boosters effectively restore antibody levels, the rate and extent of antibody decay following booster administration remain subjects of active investigation [7]. Understanding the duration of booster-induced protection is crucial for determining optimal intervals between doses and for guiding policy decisions regarding future booster campaigns [8]. Various factors influence the decay of antibodies, including age, underlying health conditions, and vaccine type [9].

Older adults and individuals with compromised immune systems may experience a faster decline in antibody levels, necessitating tailored booster strategies to ensure ongoing protection [10]. Ongoing research is exploring cellular immunity since antibodies are just one aspect of the immune response [11]. Evaluating antibody decay post-booster is crucial for personal protection and has significant implications for herd immunity and public health [12]. Immunity duration influences the timing of additional boosters, affecting resource allocation and public compliance [13]. Understanding antibody kinetics can also guide vaccine design for extended immunity [14]. In Bangladesh, as of January 29, 2023, 150,375,086 people received their first dose, 135,108,210 completed the two-dose regimen, and 66,472,672 received a booster dose (DGHS, 2023) [15]. Due to widespread Omicron outbreaks and waning immunity post-booster, several countries now offer a fourth dose to at-risk populations. An Israeli study showed a fourth BNT162b2 dose significantly reduced short-term COVID-19 risks for those who received their third dose over four months prior [16]. This study aimed to evaluate the rate of SARS-CoV-2 antibody decay over time following booster dose administration among adult populations.

Methodology

This study was a prospective observational study performed at the Department of Biochemistry & Molecular Biology, Bangabandhu Sheikh Mujib Medical University (BSMMU) in Dhaka, Bangladesh, spanning from March 2022 to February 2023. It included 80 adult participants, aged 25 to 65, who had received their COVID-19 booster dose approximately 6 to 8 months before the study. Participants were selected through a convenient purposive sampling method. As per the inclusion criteria, adult participants who were aged 25 to 65 years, regardless of gender, and had received a COVID-19 booster dose 6-8 months before the study, were included. On the other hand, individuals were excluded if they had acute infections, systemic diseases such as chronic liver or kidney disease, were pregnant, had immunosuppressive disorders like cancer, or contracted COVID-19 after providing the first sample. This study investigated the influence of various factors, including age, sex, BMI, blood pressure, random blood sugar, SARS-CoV-2 infection status, and vaccine types, on serum Immunoglobulin G (IgG) levels against SARS-CoV-2. The study aimed to assess these variables' collective or individual effects on the immune response by analyzing them. The quantitative measurement of SARS-CoV-2 specific IgG was performed using the Chemiluminescence Microparticle Immunoassay (CMIA) with an Abbott Alinity Autoanalyzer (USA). Plasma glucose levels were estimated utilizing the Enzymatic (Hexokinase/G-6-PDH) method. The collected data were entered and processed using SPSS software version 26.0. For normally distributed numerical data, the results were presented as Mean±SD. The median, interquartile range, and numbers with percentages were used for skewed data. Quantitative and qualitative data with a skewed distribution were analyzed using the Wilcoxon Signed Rank Sum test. A P-value of less than 0.05 was considered statistically significant.

Result

Of the participants, 55% were SARS-CoV-2-infected vaccinated, and 45% were non-infected vaccinated. Infected groups had more males, while non-infected had more females. The average age was 43±10 for infected and 36±6 for non-infected. Serum IgG levels decreased by 21.3% at 6-8 months post-booster ($p<0.001$). Significant declines ($p<0.05$) in IgG were observed at 3 month's interval compared to 6-8 months ago. 20.5% at 6 months, 24.3% at 7 months, and 27.8% at 8 months. Serum IgG levels significantly declined in both genders: 12.3% in males and 10.5% in females. Comparing infection history, IgG decay was significant ($p<0.05$) in both infected and non-infected vaccinated participants, with declines of 21.3% and 28.2%, respectively. By age, IgG decreased 17.4% in those aged 25-44 and 21.5% in those aged 45-65, both significantly ($p<0.05$) over 3-month intervals. By BMI, IgG decay at 3-month intervals was 7.5% in normal weight, 17.9% in overweight, and 25.7% in obese individuals. The IgG decline was significant for overweight and obese individuals ($p<0.05$), but not for those of normal weight ($p>0.05$). Among those with comorbidities, IgG decreased by 25.6% for diabetes, 31.0% for hypertension, and 35.8% for those with both, all significant ($p<0.05$) at 3-month intervals. Serum IgG decay was 29.2% for AstraZeneca, 20.8% for Pfizer, and 16.9% for Moderna boosters. While all boosters showed reductions, the decline was significant for AstraZeneca and Pfizer ($p<0.05$), but not for Moderna ($p>0.05$).

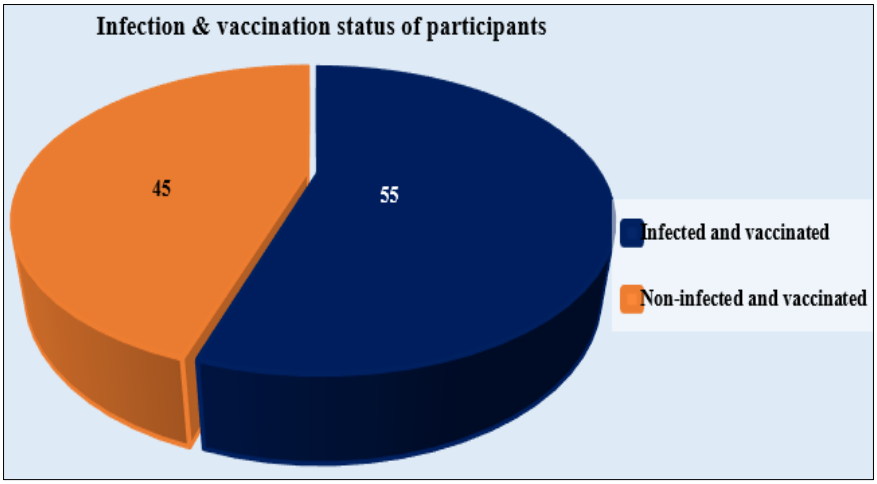

Fig 1: Pie chart showing infection & vaccination status wise participants (N=80)

Table 1: Comparison of serum IgG levels: 6-8 months post-Booster vs. 3 months' after (N=80)

Antibody IgG (AU/ml)		Decay	p-value
At initial stage	After 3 months		
Median (Range)		(%)	
2563.4	2017.9	21.3%	<0.001
(1602.4-5354.1)	(1323.5-4144.3)		

Table 2: Serum IgG levels at 6, 7, and 8 months after Booster vs. levels at 3-month intervals (N=80).

Interval	Decay	p-value
	3 months interval	
(Month)	(%)	
6	20.5%	0.032
7	24.3%	0.026
8	27.8%	0.002

Table 3: Comparison of serum IgG level (AU/ml) based on Gender (N=80).

Gender	Decay	p-value
	3 months interval	
	(%)	
Male	12.3%	0.001
Female	10.5%	0.005

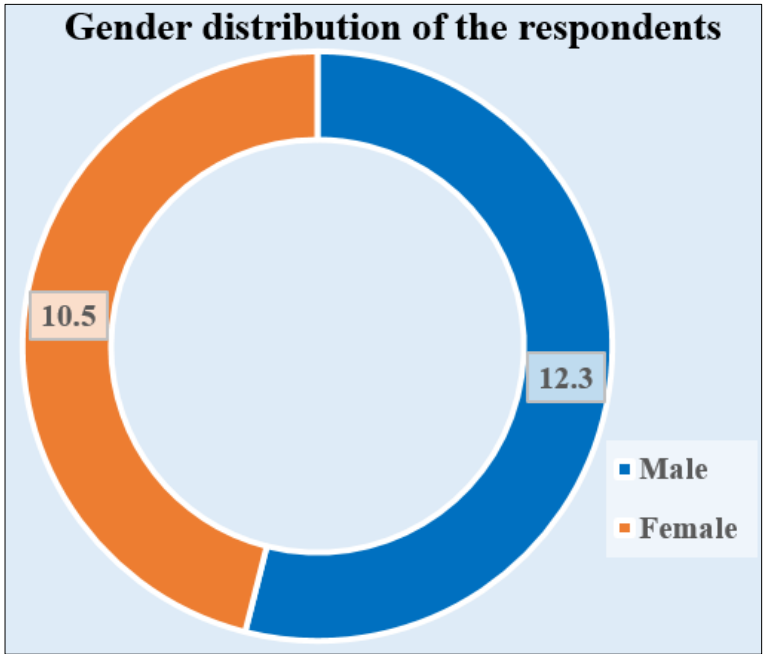

Fig 2: Ring chart showing gender wise participants decaying percentage (%) of serum IgG level (N=80)

Table 4: Comparison of serum IgG level (AU/ml) based on age group (N=80).

Age	Decay	p-value
	3 months interval	
(Year)	(%)	
25-44 Yrs.	17.4%	<0.001
45-65 Yrs.	21.5%	0.004

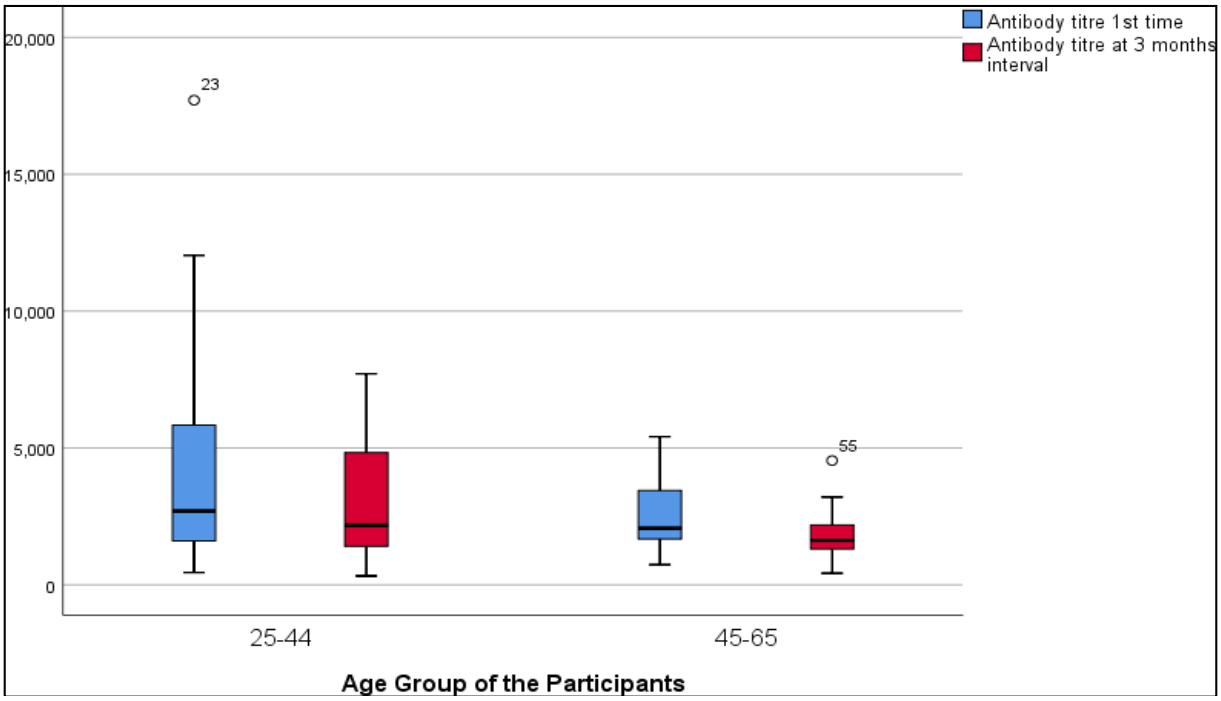

Fig 3: Box and Whisker plot showing the distribution of serum IgG level (AU/ml) in the study subjects as per the age groups

Table 5: Comparison of serum IgG level (AU/ml) according to Body Mass Index (N=80).

BMI	Decay 3 months interval (%)	p-value
Normal	7.5%	0.301
Over	17.9%	0.030
Obese	25.7%	<0.001

Table 6: Comparison of serum IgG level (AU/ml) according to the comorbidity (N=80).

Comorbidities	Decay 3 months interval (%)	p-value
DM	25.6%	0.023
HTN	31.0%	0.005
DM & HTN	35.8%	0.028

Table 7: Comparison of s. IgG levels based on vaccine and booster doses in study subjects (N=80).

Vaccines	Decay (%)	p-value
AstraZeneca 3 times	29.2%	0.026
AstraZeneca 2 times +Pfizer	20.8%	<0.001
AstraZeneca 2 times + Moderna	16.9%	0.068

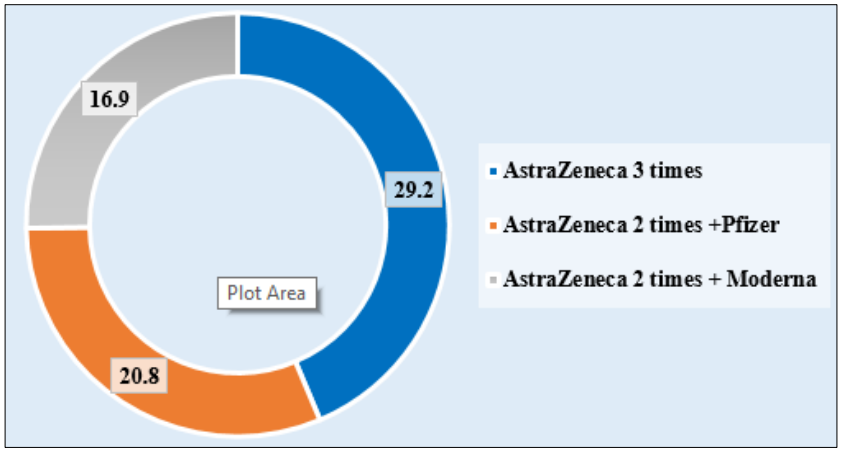

Fig 4: Ring chart showed comparison of s. IgG decaying percentage (%) levels based on vaccine and booster doses (N=80)

Discussion

This study assessed serum IgG levels 6-, 7-, and 8 month's post-vaccination, finding levels of 3350.2, 2886.3, and 2690.1 AU/ml, respectively, with higher antibody levels at 6 months. Another study [17] reported IgG declined from 12,406.0 AU/ml at 3 months to 5550.6 AU/ml at 6 month's post-booster. In our study, average IgG levels between 6-8 months were 2451.7 AU/ml in males and 2744.4 AU/ml in females, with females showing higher levels. Similarly, Phyu Pyar (2022) [18] found higher anti-spike antibody levels in females (4857.67 U/ml) compared to males (3427.78 U/ml) after three vaccine doses. Infected-vaccinated individuals had higher antibody levels than non-infected ones due to the natural immunity boost from infection. Phyu Pyar (2022) [18] also found higher anti-spike antibodies in infected cases. In our study, IgG levels were 2125.9 AU/ml for infected and 1779.3 AU/ml for non-infected individuals, with declines of 21.3% and 28.2%, respectively, consistent with Vicenti *et al*. (2021) [19] who noted faster antibody decay in non-infected individuals. The study also observed that antibody decay in normal-weight individuals was not statistically significant, while obese participants showed a significant decline, with IgG levels dropping by 7.5% in normal-weight, 17.9% in overweight, and 25.7% in obese individuals over three months. A previous study [20] found higher antibody titers in overweight and obese healthcare workers six months after two AstraZeneca doses. Another study [21] observed IgG levels decreasing in normal-weight, increasing in overweight, and declining in obese individuals, similar to our findings. Among 63 participants aged 25-44 and 17 aged 45-65 in our study, median IgG levels post-booster was 2694.4 AU/ml for the younger and 2069.6 AU/ml for the older group. After three months, levels decreased by 17.4% in the younger and 21.5% in the older group. Another study [20] noted faster declines and ongoing immune weakening in older individuals. Participants with diabetes or hypertension in our study had slightly lower IgG levels compared to non-diabetic and normotensive individuals. This aligns with Soegiarto *et al*. (2022) [22], who found lower antibody titers linked to hypertension in healthcare workers. In three months, IgG levels declined by 25.6% in diabetic, 31.0% in hypertensive, and 35.8% in those with both conditions. Singh *et al*. (2022) [23] also reported significantly lower titers in hypertensive individuals after six months compared to normotensive ones. All 80 study participants initially received AstraZeneca doses. For the booster, 8 received AstraZeneca, 49 received Pfizer, and 23 received Moderna. Median IgG levels six to eight months post-booster were 2218.7 AU/ml for AstraZeneca, 2692.8 AU/ml for Pfizer, and 3014.5 AU/ml for Moderna, with slightly higher levels observed for Pfizer and Moderna. Albanesi *et al*. (2022) [21] found that mRNA vaccines (Pfizer and Moderna) are highly immunogenic, with Moderna producing slightly higher IgG levels than Pfizer. A regimen of AstraZeneca followed by Moderna or Pfizer was more effective in inducing SARS-CoV-2 specific IgG compared to two AstraZeneca doses. Sarker *et al*. (2022) [24] reported higher antibody responses for mRNA vaccine recipients over those receiving AstraZeneca in Bangladesh. Similarly, Brunner *et al*. (2022) [25] found that 8.4 month's post-vaccination, Moderna yielded higher antibody levels than Pfizer, aligning with our findings. Antibody decay was observed across all booster vaccines over three months. The decline in antibody levels was significant for AstraZeneca (29.2%) and Pfizer (20.8%), but not for Moderna (16.9%). Mishra *et al*. (2021) [20] observed a significant antibody decline six months after two AstraZeneca doses in healthcare workers. Singh *et al*. (2022) [23] also reported significant decreases in Covishield AstraZeneca antibody titers after six months. Pareek *et al*. (2022) [26] found a significant reduction in IgG titers seven months after a Pfizer booster, although they did not assess neutralizing antibodies.

Limitation of the study

This prospective observational study had limitations due to its small sample size and limited duration. Longer follow-up periods would have been beneficial. The study's focus on a specific group from a single center limits its generalizability. Furthermore, the presence of asymptomatic SARS-CoV-2 infected individuals may have introduced bias affecting the results.

Conclusion & Recommendation

After a booster dose, antibody levels, especially serum IgG declined significantly at three month's interval who had taken booster dose within six to eight months before. This decline occurs across various demographics and health conditions, including age, gender, infection status, vaccination status, BMI, diabetes, and hypertension. While all booster types showed a reduction in IgG levels, the decline was insignificant with the Moderna vaccine, suggesting variability in antibody persistence by vaccine type. This highlights the importance of considering vaccine-specific responses for optimal booster strategies.

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Conflict of interest: None declared.

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