Original Article

Comparison of Antibody Status Following COVID-19 Vaccination between SARS-Cov-2 Infected and Non-infected Healthcare Professionals of Bangabandhu Sheikh Mujib Medical University (BSMMU), Bangladesh

Rimpi Romana[1], Forhadul Hoque Mollah[2], Tanha Waheed Brishti[3], Miliva Mozaffor[4], Abu Sadat Mohammad Nurunnabi[5], Ismet Zarin[6]

[1] *Department of Biochemistry, Ahsania Mission Medical College, Uttara, Dhaka-1230, Bangladesh;*
[2] *Department of Biochemistry and Molecular Biology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka-1000, Bangladesh;*
[3] *Department of Biochemistry, Green Life Medical College, Dhaka-1205, Bangladesh;*
[4] *Department of Biochemistry, Medical College for Women & Hospital, Uttara, Dhaka-1230, Bangladesh;*
[5] *Dalla Lana School of Public Health, University of Toronto, ON, Canada;*
[6] *Department of Clinical Pathology, Kurmitola 500 Bed General Hospital, Dhaka Cantonment, Dhaka-1206, Bangladesh.*

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Abstract

Background: Antibody developed through COVID-19 vaccination plays a vital role in combating further infection and suppressing pathogenesis of SARS-CoV-2. This study aims to observe the difference in antibody status between COVID-19 infected and non-infected healthcare professionals following two doses of COVID-19 vaccine.

Methods: This cross-sectional, analytical study was conducted in the Department of Biochemistry and Molecular Biology of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, between March 2021 and February 2022. A total of 70 adult participants (healthcare professionals) were included in this study from different departments of BSMMU Hospital. Study participants were categorized into two groups; each group had 35 participants. Group A includes healthcare professionals who were infected by SARS CoV-2 and later vaccinated by two doses of AstraZeneca COVID-19 vaccine, while Group B consists of those who were not infected by SARS CoV-2 but took two doses of AstraZeneca COVID-19 vaccine. We collected participants' demographic profile and detailed history including co-morbidities and related test results in the data collection sheet. Serum IgG was assessed by chemiluminescent microparticle immunoassay method.

Results: Serum IgG levels were found in group A as a median 2183.2 AU/ml with an IQR (inter quartile range) of 3852.0 AU/ml, while in group B, median was 624.7 AU/ml and IQR was 621.1 AU/ml ($p<0.001$). Moreover, participants having comorbidities also showed differences in IgG levels (group A median 2183.20 AU/ml, and IQR of 4095.70 AU/ml; group B median 624.70 AU/ml and IQR of 558.80 AU/ml) ($p<0.001$). Similarly, among participants with no comorbidities significant differences in IgG levels were observed (group A median 2394.45 AU/ml, and IQR 3450.73 AU/ml; group B median 653.10 AU/ml, and IQR 990.13 AU/ml) ($p<0.001$).

Conclusion: To conclude, antibody status (serum IgG levels) was found significantly higher in previously infected vaccinated group (group A) compared to non-infected vaccinated group (group B).

Introduction

The COVID-19 pandemics caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), spread across every continent since the end of 2019. By the end of February 2022, more than 400 million confirmed cases and 5.9 million deaths have been reported worldwide.[1] Since scientists have been trying their best to invent effective drug against COVID-19, none has come to the effect to date. Under the circumstances, the only strategy to protect the human being from the curse of COVID-19 is producing sufficient antibody either by low level passive exposure or active exposure to SARS-CoV-2 infection or vaccination or both.[2] Vaccination constitutes an effective strategy for the control of infectious disease; based on that strategy, COVID-19 vaccine developed by Oxford University, UK and AstraZeneca got interim recommendation for its use by the World Health Organization (WHO).[3] Bangladesh started its nationwide administration of COVID-19 vaccine on February 7, 2021 with Oxford-AstraZeneca which was manufactured and distributed by the Serum Institute of India (Covishield).[4] Evidence showed that the efficacy of the vaccine is 76% at preventing symptomatic COVID-19 beginning at 22 days following the first dose and 81.3% after the second dose.[5] The vaccines act by generating anti S protein IgG and virus specific neutralizing antibody which

Corresponding Author:
Dr. Abu Sadat Mohammad Nurunnabi
Dalla Lana School of Public Health,
University of Toronto, ON, Canada.
Email: shekhor19@yahoo.com

neutralized SARS-CoV-2 infection.[6] Apart from that previous SARS-CoV-2 infection stimulates rapid production of antibodies similar to other respiratory infections.[7] Hence, we assume that differences must prevail in antibody status between SARS-Cov-2 infected and non-infected persons after getting initial two doses of COVID-19 vaccines.

Healthcare professionals are among the highest-risk populations prone to COVID-19 infection. They were vaccinated with a priority basis according to the recommendation of the World Health Organization (WHO).[3] Following vaccination, antibody testing is vital to inform understanding of the prevalence of SARS-CoV-2 virus in the general population or in a specific group. It is important for understanding response of the vaccine to emerging variants, detecting differences in levels of immunity (vaccinated immunity versus infection-acquired immunity) and their durability.[8] The other importance is that antibody screening will inform the need for boosters and vaccination strategies in community settings.[9] Moreover, quantitative data on antibody are particularly important for studies aiming to understand the antibody response to natural infection and vaccination and to determine whether a person is further eligible to donate convalescent plasma.[10] Nonetheless, are available in our country about post vaccination antibody status with or without previous SARS-CoV-2 infection in general population or in any high-risk group. Hence, we proposed this cross-sectional, analytical study to evaluate and compare the antibody status between SARS-CoV-2 infected vaccinated and SARS-CoV-2 non-infected vaccinated healthcare professionals working in our institution (Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh).

Methods

This cross-sectional, analytical study was conducted in the Department of Biochemistry and Molecular Biology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, between March 2021 and February 2022. Based on inclusion and exclusion criteria, a total of 70 healthcare professionals were included in this study from different departments of BSMMU Hospital.

Inclusion criteria:

1) Aged between 25 and 65 years;
2) Healthcare professionals who were SARS-CoV-2 infected last 8-12 months ago (RT-PCR positive report) and received two doses of AstraZeneca COVID-19 vaccine 4 to 6 months back; and
3) Healthcare professionals who were SARS-CoV-2 non infected but received two doses of AstraZeneca vaccine last 4 to 6 months ago.

Exclusion criteria:

1) Subject with acute infection;
2) Pregnant women;
3) Lactating mother;
4) History of heart failure;
5) Chronic systemic diseases, e.g., chronic liver disease, chronic kidney disease; and
6) Subject who are suffering from any immunosuppressive disorders e.g., cancer, SLE, etc.

Study participants were categorized into two groups; there were 35 participants in each group. Group A includes healthcare professionals who were previously infected by SARS CoV-2 and later vaccinated (two doses of AstraZeneca COVID-19 vaccine), while Group B consists of those who were not infected by SARS CoV-2 but received the same doses of AstraZeneca COVID-19 vaccine. A data collection sheet formatted both in English and Bengali was used as a data collection tool. The sheet included three sections: section-I contained general information, while section-II contained information related to SARS-CoV-2 infection and section-III included further test reports related to this study.

After that, with all aseptic precaution, 5ml blood sample was collected from the anti-cubital vein, using a disposable plastic syringe. 2ml of blood was delivered immediately into sodium-fluoride tube (grey top tube) and 3ml into a plain tube (red top tube). All the test tubes were centrifuged properly at 3000 rpm for 10 minutes to separate plasma and serum within one hour of collection. Then the serum (about 500µml) was separated from each of the plain tube by micropipette, collected in Eppendorf tube, properly labeled, and stored at minus 65-degree Celsius temperature. Estimation of serum IgG levels was done using chemiluminescent microparticle immunoassay in Abbott Alinity i Autoanalyzer (made by Abbott Inc., USA). All immunological assays were performed in the Department of Biochemistry and Molecular Biology of Bangabandhu Sheikh Mujib Medical University (BSMMU). Autoanalyzer used in this study was calibrated before starting the tests as per test manual. Before starting daily investigations, control run was done. Quality control and quality assurance in all areas were maintained as per respective laboratory rules. Pre-analytic, analytic, and post-analytic errors were carefully minimized as per laboratory standard operating procedure (SOP).

After multiple checking, data were recorded in a predesigned data collection sheet. Continuous variables were expressed as mean±SD and compared between groups by unpaired student's t-test. Categorical variables were expressed as frequency and percentage and compared using Chi-square test. Mann-Whitney U test was done to compare serum IgG levels in between SARS-CoV-2 infected vaccinated group and SARS-CoV-2 non-infected vaccinated group. Level of significance was defined as p-value <0.05 at 95% confidence interval. Statistical analysis was done using Statistical Package for the Social Sciences (SPSS) version 20.0 for windows. Ethical clearance was obtained from the Institutional Review Board (IRB) of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh.

Results

The mean age of previously infected and vaccinated individuals (group A) was 41.14±12.51 years, while 38.43±9.18 years for non-infected but vaccinated individuals (group B). However, there was no significant difference in age between the groups (p>0.05). A male predominance was observed in group A; in contrast, female predominance was found in group B. The difference in gender between the groups was statistically significant (p<0.05). In group A, there were 57.1% doctors, 20% nurses, 8.6% phlebotomists, and 14.3% other staff, while in group B, there were 48.6% doctors, 17.1% nurses, 11.4% phlebotomists, and 22.9% other staff. No significant difference was observed between the groups (p>0.05) (Table 1). Serum IgG levels were found in group A as a median 2183.2 AU/ml with an IQR (inter quartile range) of 3852.0 AU/ml., while in group B, median was 624.7 AU/ml and IQR was 621.1 AU/ml. The difference was statistically significant between two groups (p<0.001) (Table 2, Fig. 1). Among participants having comorbidities (e.g., hypertension and diabetes mellitus) had following IgG levels: in group A as median 2183.20 AU/ml, and IQR of 4095.70 AU/ml, and in group B, as median 624.70 AU/ml, and IQR of 558.80 AU/ml. (p<0.001). Among participants with no comorbidities showed similar differences in IgG levels (group A median 2394.45 AU/ml, and IQR 3450.73 AU/ml; group B median 653.10 AU/ml, and IQR 990.13 AU/ml) (p<0.001) (Table 3).

Table 1: Demographic characteristics of the study participants (n=70)

Variables	Group A (n=35)	Group B (n=35)	p-value
Age in years			
Mean±SD	41.14±12.51	38.43±9.18	>0.05NS
Gender			
Male	24 (68.6)	14 (40.0)	<0.05S
Female	11 (31.4)	21 (60.0)	
Occupation			
Doctor	20 (57.1)	17 (48.6)	>0.05NS
Nurse	7 (20.0)	6 (17.1)	
Phlebotomist	3 (8.6)	4 (11.4)	
Other Staff	5 (14.3)	8 (22.9)	

Continuous variables were expressed as mean±SD, while categorical variables were expressed as frequency and percentage. Unpaired students t-test was used to compare differences in age, while Chi-square test was used to compare gender and occupation. S=significant, NS=not significant.

Table 2: Comparison of antibody status (serum IgG) in between infected vaccinated and non-infected vaccinated healthcare professionals (n=70)

Anti-body status (AU/ml)	Group A (n=35)	Group B (n=35)	p-value
Median	2183.2	624.7	<0.001S
IQR	3852.0	621.1	
Min - max	861.7-12884.1	96.1-2330.0	

Data were expressed as median and IQR (Inter quartile range). The p-value reached from Mann-Whitney U test; S=significant.

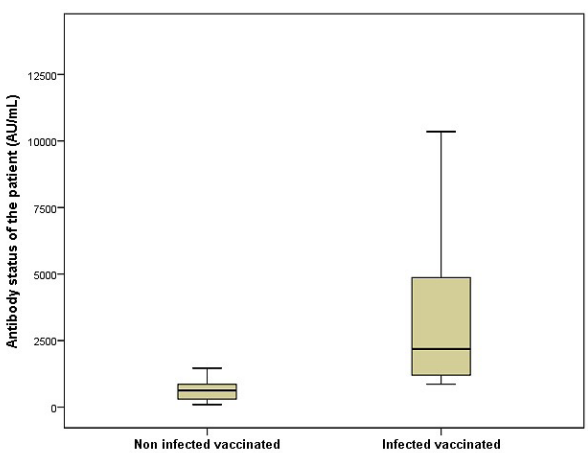

Figure 1: Distribution of IgG levels (in AU/mL) in SARS-CoV-2 infected vaccinated and SARS-CoV-2 non-infected vaccinated study participants (35 in each group).

Table 3: Antibody status (serum IgG) of the study subjects with and without co-morbidities (n=70)

Variables	Antibody status (AU/mL)	Group A (n=35)	Group B (n=35)	p -value
With comorbidity (n=26)	Median	2183.20	624.70	<0.001S
	IQR	4095.70	558.80	
	Min - max	897.30-8797.60	99.40-1393.90	
Without comorbidity (n=44)	Median	2394.45	653.10	<0.001S
	IQR	3450.73	990.13	
	Min - max	861.70-12884.10	96.10-2330.00	

Data were expressed as median and IQR (Inter quartile range). The p-value reached from Mann-Whitney U test; S=significant.

Discussion

Antibody plays a vital role in suppressing the pathogenesis of SARS-CoV-2 by disrupting the binding of viral spike protein to angiotensin-conveting-enzyme2 receptor on the target cell.[11] A longitudinal study in China showed that IgM levels increased first week after SARS-CoV-2 infection peaked 2 weeks after that decline whereas IgG was detectable after 1 week and maintained at a high level for a long period. The peripheral T and B cell from the SARS-CoV-2 patients revealed a positive correlation of humoral immune response and the T cell immune memory with disease severity.[12]

Evidence showed a strong relationship between previous SARS-CoV-2 infection and higher antibody responses. Several research reported that individuals with previous SARS-CoV-2 infection generate strong humoral and cellular responses to one dose/two doses of COVID-19 vaccine, with evidence of high titres of in-vitro live virus neutralisation. In contrast, most individuals who are infection-naive generate both weak T-cell responses and low titres of neutralising antibodies.[13-16] Evidence also showed that upon primary immunization, participants with pre-existing immunity (those who had previously been infected with the virus) mounted higher antibody responses faster and achieved higher steady-state antibody titers than individuals who had not been previously infected. The waning of antibody response was characterized by two phases: an initial rapid decay from the strong peak after vaccination, followed by a stabilization phase with very slow decay, suggesting that antibody levels were very long-lasting.[17-21] Our results are in congruence with those research fundings.

We evaluated the antibody levels with or without comorbidities among healthcare professionals; higher antibody levels were observed in individuals with no comorbidities in both infected vaccinated group and non-infected vaccinated group. Several research concluded that, following vaccination, there was significant difference in antibody levels in between diabetes, cardiovascular disease patients and normal individuals,[22-25] which align with the results observed in our study. However, some studies observed that the inequalities in antibody levels amongst those groups did not persist after the second dose.[20,23] Nevertheless, it is not yet clear how differences in antibody responses translate into changes in vaccine effectiveness, although there is suggestion that higher antibody levels are associated with better protection in terms of severe outcomes.[23]

Conclusion

To conclude, antibody status (serum IgG levels) was found significantly higher in previously infected vaccinated group (group A) compared to non-infected vaccinated group (group B). However, further studies are recommended involving larger samples from different age groups and multicentre across the country.

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Conflict of interest:

The authors declare no financial or personal competing interest.

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