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# Antibody level against Covid-19 among the vaccinated infected and non-infected doctors by SARS-COV-2: A Comparative study

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## ABSTRACT:

**Introduction:** A novel corona virus (2019-nCoV or SARS-CoV-2) emerged at the end of 2019 in Wuhan, Hubei province in China named as COVID-19. IgM, the first antibody produced by the body is generated gradually in 1 week after symptom onset and declines at 4 weeks after the COVID infection. In this background, the antibody response was observed in vaccinated (by Oxford-AstraZeneca) doctors of SSMC(Sir Salimullah Medical College) with or without previous COVID-19 infection. **Methodology:** This cross sectional analytical study was conducted in the Department of Biochemistry and Molecular Biology at SSMC and BSMMU. A total 70 doctor of SSMC aged 25-59 years were enrolled according to inclusion criteria. Among them 35 vaccinated doctors were previously infected by SARS-CoV-2 regarded as group A and another vaccinated 35 doctors were non-infected regarded as group B. Collected data was analyzed by Statistical Package for Social Science 26 (SPSS 26). The data were expressed as frequency and percentage, mean ± SD for normally distributed data or median (inter-quartile rage) for data not normally distributed. Mann-Whitney test was done to compare IgG status between vaccinated SARS-CoV-2 infected and non-infected individuals. **Result:** There was significantly higher level of antibodies (serum IgG level) present in fully vaccinated doctors with previous SARS-CoV-2 infection than in only vaccinated doctors without prior infection.

**KEY WORDS: Covid-19, vaccination, infected and Non-infected Doctors, SARS-COV-2**

## INTRODUCTION:

The Coronavirus disease – 2019 (COVID-19) is an evolving infectious disease caused by severe acute respiratory syndrome Coronavirus (SARS-COV-2). It was firstly reported in Wuhan city, Hubei province. There are several ways to transmit this virus in humans with incubation times of 2-14 days but the most possible way is the airborne transmission through droplet nuclei [1]. The entry of SARS-CoV-2 in to host cells are initiated by binding of its RBD(Receptor Binding Domain) of spike glycoprotein to the angiotensin-converting enzyme 2 (ACE2) receptor[2]. Firstly the virus enters through mucous membrane of the upper respiratory tract, later it affects the lung. The spike protein is a major target for design of vaccines and inhibitors of viral entry. It consists of two domains S1 and S2 [3]. The spike protein facilitates viral entry in to host cells by binding to a host receptor through the host cell [3]. Antibodies binding to the spike (S) protein RBD can neutralize SARS-CoV-2, covid-19 infected patients with a wide range of clinical features from mild illness to severe pneumonia[4]. The common symptomatology of these patients including fever, dry cough, sore throat, shortness of breath, mayelgia, headaches,diarrhea and insomnia. In severe causes, difficulty in breathing , need for mechanical ventilation and death can occur [5]. Yet a large number of COVID-19 infected patients remains asymptomatic [6]. The virus can infect people of all ages. Two groups of people are at a higher risk of getting severe Covid-19 disease. People over 60 years old and those with underlying medical conditions such as diabetes, chronic respiratory disease, cardiovascular complications, cancer and obesity [7]. Real time reverse transcription polymerase chain reaction (RT-PCR) for viral RNA detection is widely used for the

diagnosis of COVID-19. As there is risk of false negative results by RT-PCR method, serum specific antibody detection for COVID-19 is advisable due to its instant diagnosis[8]. After invading of virus in to the host, large amounts of immunoglobulin (Ig) are produced by the body's immune system and release them in to blood including IgG, IgM and IgA. IgG is a major class of immunoglobulin. It remains in blood comprising 75% of total serum immunoglobulin which has long term immunity and immunological memory [9]. IgM normally present at a concentration of 1-2 mg/ml of blood, with a half-life of about 5 days [10]. In response, the scientific community has made a remarkable progress, resulting in the generation of multiple vaccine, using a variety of different approaches such as the Pfizer BNT-162b2, Modena mRNA-1273, Oxfored – AstraZeneca etc [10]. More than 4.88 billion vaccine doses have been administered worldwide. As vaccine doses remain relatively insufficient globally, most countries have focused their early vaccination efforts on priority groups like the clinically vulnerable, people of older age and most importantly front line workers like doctors, nurses and other health professionals[11]. Bangladesh began administration of COVID-19 vaccines on 27 January 2021 while mass vaccination was available on 7 February 2021. So far, Oxford-AstraZeneca work better against Alpha variant than Beta variant, in case of Delta variant it is 60% effective in symptomatic cases and 93% effective against hospitalization after the completion of doses [12] In vaccinated individuals the decay of neutralizing antibody titer occur over first 3-4 months after vaccination which is as rapid as decay found in convalescent individuals [13] . Nevertheless, there are limited conception about the duration of persistence antibody after infection and vaccination, IgG antibody titer in patients with co-morbidities like hypertension, diabetes etc. and the chances of re-infection within the interval. So far literature review reveals scarce of relevant co-relational study in Bangladesh. So this study will put significance in interpreting anti SARS-CoV-2 antibody test result in COVID-19 infected and non-infected vaccinated individuals and in understanding humeral response patterns for SARS-VoV-2 infection in current and potential future COVID-19 outbreak scenarios. It is now demanding question to the physicians and researchers to know the duration of persistence and declining and declining of antibody after infection and vaccination and the antibody level that prevent symptomatic re-infection or reduce it's severity. So far Doctors are more susceptible to get infected as they are working as a front liner, having more close contact with the infected patients as well as they form an essential part of an effective response to the COVID-19 pandemic. From this study we want to give an idea about the quantitative difference of immunoglobulin produced in vaccinated doctors with or without previous COVID-19 infection, to investigate the mmunological status with co-morbidites and any chances of re-infection in these individuals. Moreover, this study will give a clue about the antibody status after few months of vaccination. Thus the accurate assessment of antibodies during a pandemic can play an important role in monitoring protective immunity, requirement of booster dose of vaccine as well as to rescue making and regain their normal livelihood.

## METHODS & MATERIALS:

The cross sectional study was conducted in Sir Salimullah Medical College and Mitford Hospital and BSMMU, Dhaka. The study was conducted over a period of one year starting from a convenient time after approval of the protocol. The study population comprised of all the doctors who were vaccinated by Oxford-AstroZenica vaccine. Apparently healthy doctors age between 25-59 years of SSMC. Doctors a total of 70 subjects aged between 25-59 years were selected for this study according to the inclusion criteria.

**Grouping of the study subjects:**

A total of 70 subjects aged between 25-59 years were selected for this study according to inclusion criteria.

Group A:35 doctors of SSMC, vaccinated and infected by SARS-CoV-2. Group B:35 doctors of SSMC, vaccinated but not infected by SARS-Cov-2.

**Study procedure:**

By purposive sampling a total of 70 doctors were selected from Sir Salimullah medical college and hospital. Ethical permission was taken from the Ethical Review Committee of Sir Salimullah Medical College and hospital. Purpose and procedure of the study was explained in details and informed written consent was taken from each study subjects. Relevant data was taken and recorded in the data collection sheet with a prefixed questionnaire by a interview of study subject. The infected vaccinated subjects were selected on the basis of RT-PCR report and vaccination certificate and non-infected vaccinated subjects were selected on the basis of only vaccination certificate. Blood samples were collected for estimation of IgG and RBS. The method of quantitative determination of SARS-CoV-2 specific IgG , was an Indirect chemiluminescence micro particle immunoassay (CMIA).

**Laboratory method:**

Estimation of serum IgG was assessed by Chemiluminescent Microparticle Immunoassay(CMIA)using Abbott Alinity i Autoanalyzer (USA). Estimation of Blood Glucose (Random) by Glucose Oxidase method

## RESULTS AND OBSERVATIONS

This cross sectional analytical study was conducted in the Department of Biochemistry and Molecular Biology, BSMMU and SSMC from March 2021 to February 2022. A total of 70 vaccinated study subjects were enrolled according to the inclusion and exclusion criteria. Among them 35 vaccinated subjects were previously infected by SARS-CoV-2 and another

vaccinated 35 subjects were non-infected. All the information was collected and tabulated in the following formats and the findings are presented in the subsequent pages.

**Table I : Grouping of the study subjects on the basis of infection by SARS- CoV-2**

| Group | Number of patients (n) | Percentage (%) |
|---|---|---|
| **Group-A:** Vaccinated and previously infected by SARS-CoV-2 | 35 | 50 |
| **Group-B:** Vaccinated and non-infected | 35 | 50 |
| **Total** | 70 | 100 |

**Table II: Age and gender distribution of study subjects (n=70)**

| Groups | Group A (n=35) | Group B (n=35) | *p* value |
|---|---|---|---|
| *Age (in years)* | | | |
| 20-29 | 4 | 2 | |
| 30-39 | 15 | 11 | |
| 40-49 | 8 | 15 | |
| 50-59 | 8 | 7 | |
| mean ± SD | 39.77 ± 10.63 | 42.54 ± 8.89 | 0.240a |
| *Gender* | | | |
| Male, n (%) | 18 (52%) | 16 (46%) | |
| Female, n (%) | 17 (48%) | 19 (54%) | 0.632[b] |

Results were expressed as mean ± SD, frequency (n) and percentage (%).
Unpaired student's 't' test was done to measure the level of significance.
Chi-square test was done to measure the level of significance.
Here p value <0.05 is considered as significant.

**Table II** showed age and gender distribution of study subjects among groups. The mean age of group A was 39.77± 10.63 years and group B was 42.54 ± 8.89 years. There were no significant differences in terms of age and gender between two groups.

**Table III : Comparison of the antibody (serum IgG) level between vaccinated infected and non-infected individuals (n=70)**

| | Group A (N=35) | Group B (N=35) | *p* value |
|---|---|---|---|
| Median with range of IgG (AU/ml) | 2418.10 (1285.8 – 5127) | 426.4 (251.1 – 682.4) | .00001 |

Mann-Whitney U test was done to measure the level of significance.
Level of significance p <0.05.
Data were expressed as median (Inter Quartile Range, IQR).

Table III showed the median value of IgG regarding Group A (infected and vaccinated) was 2418.10 and Group B (non-infected and vaccinated) was 426.4. Mann-Whitney U test was done to analyze the data which revealed presence of significantly higher antibody (IgG) in SARS-Vov-2 infected vaccinated group in comparison to non-infected vaccinated group. P value<0.00001 was considered as significant.

**Table IV : Comparison of SARS-CoV-2 Antibody (Serum IgG) level among the study subjects with and without co-morbidities (n=70)**

| Comorbidities | | Infected vaccinated | Non-infected vaccinated | *p value* |
|---|---|---|---|---|
| Present | Median with range of IgG (AU/ml) | 2626.8 (1268.8 – 4031.7) | 330.2 (238.2 – 490.6) | **0.00056** |
| Absent | Median with range of IgG (AU/ml) | 2225.2 (1857.1 – 5826.9) | 445.7 (341.9 – 1060.5) | **0.00672** |

Data were expressed as median (Inter Quartile Range, IQR).
Mann-Whitney U test was done to measure the level of significance.
Level of significance p <0.05.

**Table IV showed** comparison of antibody level between co-morbidities and without co-morbidities among previously infected and non-infected individuals. Mann-Whitney U test was done to analyze the data which revealed that significantly higher (p < 0.05) IgG was present in both previously SARSCoV-2 infected comorbid & non-comorbid doctors than non-infected comorbid & non-comorbid vaccinated doctors.

## DISCUSSION

In this study, it was observed that SARS-COV-2 was more in males than females. Here vaccinated and SARS-COV-2 infected males were 52% and only vaccinated but non-infected were 48% and 54% respe ctively. But there were no significant differences in terms of gender between two groups.

The present study showed that in both groups, a considerable number of study subjects were suffering from hypertension and diabetes. Here 33.7% were hypertensive, 30.5% were diabetic and 21.8% were both hypertensive and diabetic participants in Group A. In contrary, 67.4% vaccinated and non-infected participants had no history of co-morbidity. But there were no significant differences in terms of gender between two groups. This study was relevant with a recent observational study in Italy done by Raimondi et al.[14], which mentioned that no significant differences were observed between female and male (26% Vs. 38%) respectively. Another cross sectional study stated that there was increased number of infected patient despite no identified co-morbidities. However it is noted by several studies in many countries that the patients with co-morbidities have more deteriorating outcomes compared with patients without co-morbidity [15].

In this current study, the IgG level was analyzed between vaccinated SARS-CoV-2 infected and vaccinated non-infected groups and the relative value of IgG (in median IQR) was found significantly higher in vaccinated and SARS-CoV-2 infected group [2418.10 (1285.8-5127), p <0.00001] than vaccinated non-infected participants [426.4

(251.1-682.4)]. The value of IgG was almost 6 fold higher in vaccinated and SARS-CoV-2 infected group. This finding was in agreement with Krammer et al.[16]. This study showed that the antibody titer (IgG level) of vaccinees with pre-existing immunity were 10 to 45 times as high as those of vaccinees without pre-existing immunity at the same time. Similarly, a study done by Callegaro et al.[17] in Italy reported that vaccines elicits a very strong immune response in seropositive individuals with antibody titer almost 10 fold higher to those without past SARS-CoV-2 infection. A retrospective observational study in Israel was done by Gazit et al.[18] which mentioned that natural immunity provided stronger and longer lasting protection against infection, symptomatic disease and hospitalization caused by Delta variant of SARS-CoV-2[19]. Suggested that the presence of anti-spike or anti-nucleocapsid IgG were associated with the less chance of SARS-CoV-2 re-infection in the next 6 months. Another study done by Heidi Ledford [20] found that about 90% protections against re-infection as much as a year after about of SARs-CoV-2.

In this current study, the value of IgG (in median IQR) of male doctors were [1263.10 (439.67-3191.62)] and female doctors were [ 962.25 (445.2-1625.37) ]. In both groups, the IgG level between male and female revealed no statistically significant difference. A recent study in USA by Takahashi et al. [21] determined the immune responses against SARS-CoV-2 infection in male and female patients. There were no differences in the amount of IgG between male and female patients.

In this present study, the level of IgG (in median IQR) between co-morbidity and non-comorbidity among previously infected group were [2626.8 (1268.8-4031.7)] and [2225.2 (1857.1-5826.9)] respectively. The value of IgG was found significantly higher in both previously SARS-CoV-2 infected co-morbid and non-comorbid doctors than non-infected group. In a study of UK, Barin B et al.[22] documented that, a significantly higher level of IgG titer was observed in individuals those were infected severely or critically by SARS-CoV-2 with or without any identified co-morbidities, which was consistent with our study. Furthermore, in case of mild or moderate disease with co-morbidity individuals had significantly higher IgG level[22]. A retrospective study in China showed serum antibodies in patients with co-morbidity where serum IgG persisted at a high level up to 8 weeks[23].

The correlation between age and IgG in this current study showed weakly negative but statistically insignificant (p >0.05) association between age and antibody status (IgG level) in both groups.

There existed some reports, proposing difference of antibody status between vaccinated SARS-CoV-2 infected and non-infected groups, although with some conflicting results. It was remarkable that age plays an imperative role in COVID-19 infection as general immunity reduces with increasing age. Many were in agreement with the fact that, male gender is one of the predictors for COVID-19 infection. Moreover, a significant higher level of IgG titer was revealed in individuals infected by SARS-CoV-2 with or without presence of co-morbidity. Findings of this study observed that serum level of antibody was significantly higher in COVID vaccinated doctors those were infected by SARS-CoV-2 compared to COVID vaccinated doctors without SARS-CoV-2 infection.

The present study concluded that there were significantly higher levels of antibodies (serum IgG level) present in fully COVID vaccinated doctors with previous SARS-CoV-2 infection than in only COVID vaccinated doctors without prior infection.

## CONCLUSION:

The present study concluded that there were significantly higher levels of antibodies (Serum IgG level) present in fully COVID vaccinated doctors with previous SARS-CoV-2 infection than in only COVID vaccinated doctors without prior infection. so a study should be designed to find out the duration of persistence and declining of antibody after infection and vaccination as well as to find out the effect of booster dose of vaccine among the study subjects.

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