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Comparison of Covid-19 IgG Anti-Spike Antibody Titer after Vaccination with Sputnik V in Seropositive and Naïve Vaccinees

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ABSTRACT

Introduction: Immunity to SARS-CoV-2 has shown to reduce the risk of having a severe infection and initiate a good degree of disease protection. **S**tudies assessing the antibody titer after vaccination can be very helpful to see whether previously infected individuals have better immunological response as compared to uninfected or antibody naïve individuals.
Aims & Objectives: Comparison of Anti-spike IgG antibody among vaccinees with or without previous exposure to COVID-19. To determine whether single dose regimen can produce significant antibody titer amongst previously infected cases and design vaccine dosage regimens accordingly.
Place and duration of study: This study was conducted at Chughtai Institute of Pathology from April 2021 to June 2021.
Material & Methods: Blood samples were collected from 83 adult male and female vaccinees at baseline, 3 weeks after the first dose and finally 7 days after the second dose. Previously infected individuals' record was noted separately. Samples were immediately analyzed using Abbott SARS-CoV-2 IgG II quant two step immunoassay. Data was analyzed using SPSS 23.0. A p-value of <0.05 was considered significant.
Results: Majority of the candidates (57 %) were females and on analysis it was found that 42% of the patients were seropositive whereas 58% of the patients were antibody naïve before receiving the first dose of vaccine. There was a significant difference between mean antibody titer of seropositive and seronegative study participants at day 0, day 21 and finally on day 28 (p value <0.001) with seropositive individuals having higher antibody titers even after first vaccine shot.
Conclusion: Post vaccination immunological response was higher in seropositive individuals as compared to the antibody naïve and this finding can help the policy makers to design a single dose vaccine regimen for the former category.

Key words: COVID-19, Sputnik V, Antibody, IgG, Vaccine

INTRODUCTION

The emergence of COVID-19 has led to one of the most ambitious vaccination programs ever. Immunity to SARS-CoV-2 either induced via a natural infection or vaccination has shown to reduce the risk of having a severe infection and initiate a good degree of protection against getting reinfected.[1] Seropositivity against SARS-CoV-2 has ensured a reasonable protection of more than 80% from reinfection.[2] On the other hand, around 60-95% efficacy of vaccines have been reported and countries around the world are racing to vaccinate individuals against SARS-CoV-2.[3] The duration of effective immunity, either via natural infection or vaccines, still remains unclear and the only evidence available is presence of primary immune responses.[4] Another concern is the emergence of viral variants that may be resistant to both vaccine induced and convalescent immune response.[5]

In Pakistan, the vaccine drive started early in 2021 with more than 4 million people fully vaccinated till mid of July.[6] Pakistan has so far approved eight COVID vaccines; Sinopharm, Cansino, Sinovac, Sputnik, AstraZeneca, Pakvac, Moderna and Pfizer. Phase 3 trials of these vaccines showed reasonable efficacy at preventing severe infection after two doses (or one if single dose vaccine) administered at fixed time interval. A summary of these vaccines is given in Table-1.

Company	Type of Vaccine	Mechanism
Sinopharm	Inactivate Viral Vaccine	Virus killed by heat/chemicals
Cansino	Viral Vector vaccine	A harmless Virus transports Virus gene
Sinovac	Inactivated Viral Vaccine	Virus killed by heat/chemicals
Sputnik	Viral Vector vaccine	A harmless Virus transports Virus gene
AstraZeneca	Viral Vector vaccine	A harmless Virus transports Virus gene
Pakvac	Inactivated Viral Vaccine	Virus killed by heat/chemicals
Moderna	RNA Vaccine	mRNA template for Viral proteins
Pfizer	RNA Vaccine	mRNA template for Viral proteins

Table-1: Vaccines along with their mechanism of action

Vaccination drive in Chughtai Lab started in March 2021 and two doses of Sputnik V were administered intramuscularly, three weeks apart. Sputnik V is an adenovirus viral vector vaccine developed by Gamaleya Research Institute registered on 11 August 2020 by the Russian Government. Clinical trials have shown a strong protective immunological response of Sputnik V across all age groups. This vaccine uses adenovirus 26(Ad26) and adenovirus 5(Ad5) as vectors for the expression of SARS-CoV-2 spike protein.[7] An efficacy of 91.6% was reported after the first dose of Sputnik V in a Russian Study and an evidence of reduced disease severity is encouraging for the supporters of dose sparing strategy.[7]

In a developing country like Pakistan, with limited resources, studies conducted to look for the antibody titer after vaccination can be very helpful to assess the efficacy of vaccines and the immunological response after first and second shots. This will help to design the dosage regimens accordingly. The persistence of vaccine induced antibody level is still not known, however, infection induced antibodies tend to remain detectable almost 6 months after infection.[8] Studies show that individuals who have been infected with corona virus can safely skip the second jab of two dose vaccines, however the concern lingers.[9]

Ideal vaccine dosage regimens have not yet been designed separately for those who have been naturally infected and those who have not been exposed by the virus or are antibody naïve. We designed this study to see whether previously infected individuals had better immunological response as compared to uninfected or antibody naïve individuals. This study can also help us to assess whether previously infected individuals could establish recall responses to single shot of vaccine and the unadministered doses can be saved for rest of the population.

MATERIAL AND METHODS

This cross-sectional study was conducted at Chughati Institute of Pathology from April 2021 to June 2021. Ethical approval was obtained from the Institutional Review Board under letter number CIP/IRB/1066. Blood samples were collected from 83 adult male and female patients who booked for the vaccine shot after an informed consent. Patients were not charged for the antibody test, however they paid for the vaccination. Blood samples were collected at baseline, 3 weeks after the first dose and finally 7 days after the second dose. Blood was only collected at 7 days after the second dose and not after the 14th and 30th days because of lack of compliance of the patients. Most of the patients could not be traced after 7 days of the second dose.

At the time of sample collection, participants were asked whether they were previously infected by SARS-CoV-2, confirmed via RT-PCR or not and details were recorded on a predesigned proforma. Patients who had history of autoimmune diseases, rheumatoid arthritis, active coagulopathy, SARS-CoV-2 RT-PCR positive results within last 15 days and those who received plasma transfusion, blood transfusions or muromonab antiCD3 antibody (OKT3) were excluded from the study. Three ml blood was collected on 0, 21 and 28 days and centrifuged at 3000 RPM for analysis. Samples were immediately analyzed after collection using fully automated analyzer Alinity ci by Abbott Diagnostics. Immediate processing was possible because vaccination drive was carried out at the Head Office and research samples were taken where the analyzer was present. The Abbott SARS-CoV-2 IgG II quant two step immunoassay used in this study uses chemiluminescent microparticle immunoassay technology designed to quantify IgG antibodies (including neutralizing antibodies) to the receptor binding domain (RBD) of S1 subunit of the SARS-CoV-2 spike protein in human serum or plasma.[10] Anti-Spike IgG level of 7.1 BAU/mL (Binding Antibody unit/mL) was taken as cutoff value according to the manufacturer's protocol. Levels>7.1 BAU/mL were considered as seropositive.[11]

Statistical analysis:

Data was analyzed using SPSS 23.0. Frequencies and percentages were calculated and mean antibody

titer between groups was compared using t test. p value <0.05 was considered significant.

RESULTS

Our study group comprised of 83 candidates; 57% (n=48) were females and 43% (n= 35) were males. A total of 30 patients were RT-PCR confirmed SARS-CoV-2 positive at least 30-60 days prior to first dose of vaccine on the basis of history they gave. On analysis it was found that 42% of the patients were seropositive whereas 58% of the patients were antibody naïve before receiving the first dose of vaccine. The percentage of seropositive patients before getting the first shot of vaccine was greater as compared to those who gave a history of being infected showing that some of the participants were infected without having symptoms or had very mild symptoms and never got tested. Mean age of seropositive patients was 35.4 (±9.1) years and mean of antibody naïve vaccinees was 38.02 (±12.9) years (p-value 0.325). We finally divided the study participants on the basis of seropositivity and compared the mean antibody titer between seropositive and seronegative study participants at Day 0 (on the day of first vaccine dose), Day 21 (on the day of second vaccine dose before getting vaccinated) and finally on Day 28 (7 days after getting the second vaccine dose). It was found that a significant difference was present in the antibody titers of the two groups. (Table-2)

Days of analysis	Mean Antibody titer seropositive group (BAU/mL)	Mean Antibody titer seronegative group (BAU/mL)	p-Value
Day zero*	175.08	3.03	<0.001
Day 21**	2333.47	191.07	<0.001
Day 28***	2253.04	744.02	<0.001

Table-2: Comparison of Mean antibody levels at different time intervals between study groups

*On the day of first dose of vaccine before getting vaccinated
**21 days post first dose of vaccine before getting second shot
***7 days after second shot of vaccine
BAU/mL: Binding antibody Unit per mL

DISCUSSION

COVID-19 emergence led to a rapid development of multiple vaccines based on different techniques. The Government of Pakistan started this vaccination drive after the vaccines were declared safe to use by the WHO. Chughtai Institute of Pathology initiated this drive to fulfill the huge requirement of population getting vaccinated in the private sector. Our in-house vaccination enabled us to start an independent follow up study of vaccination induced immunity. In the present study, we observed a significant difference in the immune response of seropositive and seronegative candidates, both groups responding to the first dose of vaccine producing detectable antibodies. The second dose given according to the designed vaccine protocol induced higher levels of antibodies in the seropositive subjects as compared to the seronegative individuals.

The vaccine induced immune response is found to be higher in patients having severe disease course as compared to those having asymptomatic disease according to latest studies.[12-14] In this study, we did not stratify the patients according to the disease severity, therefore we couldn't comment on the correlation of severity of infection with the antibody titer. However, there was a considerable increase in the titer after the second dose which is in accordance with the study performed by Jalkanen et all.[15] Saadat et al observed a better immunological response among the previously seropositive vaccinees on a single vaccine dose as compared to the seronegative ones and this finding is similar to our study.[16] The authors of the aforementioned study suggested a single dose vaccination strategy or low priority stratification for previously infected individuals due to the worldwide vaccine shortage.[17] A recent study showed findings similar like to our study; Previously infected study participants had higher titers of anti-spike antibody as compared to those without having any history of infection. At baseline, no antibodies were detected in the group without history of infection, however, the seropositive individuals had significantly higher level of antibodies as compared to the seronegative group at various time intervals during the study. Authors of this study also mentioned that a single vaccine dose was enough to develop significant vaccine titer in the seropositive group.[18] Lombardi et al reviewed antibody titers among vaccinated health care workers and stratified the results on the basis of previous history of infection. The researchers found that the health care workers who were infected more than 6 months before getting vaccine had significantly higher titers of antibody as compared to those who were infected less than 6 months before vaccination and the uninfected study subjects had the lowest titers of antibodies.[19] Higher antibody titers among previously infected individuals is an expected finding as the vaccine acts a booster of natural immunity. Many studies show similar findings and some of the reasons given by researchers include multiple exposures to SARS-CoV-2 acting as natural boosters and vaccination at longer intervals after getting naturally infected

leading to higher anamnestic response.[20-23] Researchers have also demonstrated that single dose vaccination is able to elicit anamnestic response in seropositive individuals and these antibodies are capable of neutralizing heterologous antigen effectively.[24]

Owing to the scarce vaccine supply and financial constraints in underdeveloped world, many studies were conducted to see whether a single dose is enough for pre-infected individuals or not. Many of those studies showed that second jab of a two-dose vaccine regimen can be easily skipped for the pre-infected cases owing to high antibody titers after a single dose. Our study also revealed similar findings and it can be suggested that one dose regimen can be used for seropositive individuals, however, more evidence is still required.

CONCLUSION

Though on a limited scale, our study showed seropositive vaccinees to have a significantly higher antibody titer as compared to seronegative subjects owing to anamnestic response of naturally infected individuals. These findings can be used by health policy makers to develop a single dose vaccine regimen for selected population and better use of health finances in a developing country like Pakistan.

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