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Immunogenicity of the BBIBP-CorV Vaccine; An Observational Study from Pakistan

Zunera Jahanzeb[1], Arslan Zahid[2], Hafeez-ud-din[3], Hina Aslam[4], Samia Kausar[5], Muhammad Israr[6]

[1,3]Assistant Professor of Medicine, [2]Senior Registrar Medicine, [4]Senior Registrar Surgery,
([HBS Medical and Dental College Islamabad)
[5]Associate professor Medicine, Islamic International Medical College and Trust Rawalpindi
[6]Registrar Pulmonology, Pakistan Institute of Medical Sciences Islamabad

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Address of Correspondent
Dr. Arslan Zahid
Senior Registrar Medicine
HBS Medical and Dental College
Islamabad
azkyani@gmail.com

ABSTRACT

Objective: To determine the levels of anti-spike protein (S) antibody against SARS-CoV-2 among Vaccinated Healthcare workers of Islamabad.

Methodology: Cross-sectional Observational study carried out at HBS General Hospital from March 2021 till May 2021 involving healthcare workers from HBS General Hospital, Rawal General Hospital, Polyclinic Hospital and PIMS. The non-probability sampling technique was used. The study included male and female healthcare workers over the age of 18 who had received their second dose of vaccine at least 2 weeks before sample collection and no more than 8 weeks before sample collection.

Results: The study included 123 participants, of whom 6.5% did not have a detectable level of the antibody. The Male to Female ratio was 1.277:1 while mean age was 42.93±13.234 years. Side-effects were experienced by 42.3% (n=52) participants. Significantly higher levels of the antibody were observed in participants who had previous SARS-CoV2 infection and those who experienced vaccine side-effects.

Conclusion: The BBIBP-CorV vaccine elicited immunogenicity, leading to detectable anti-spike protein S antibody levels in 93.5% of the patients in our study.

Keywords: Anti-Spike, COVID-19, Pandemic, Vaccination.

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Introduction

The world as we know it changed early last year. The COVID-19 pandemic ravaged the globe, starting from China and spreading across the whole world. Once called "Social Animals", humanity has been forced into a social withdrawal by this pandemic, as it takes its toll not only as the lives of the departed but also on the physical and mental debility of the survivors while the uninfected live in continuous fear and relative solitude. More than a year since its beginning, the pandemic has taken 4.2 million lives and has affected more than 200 million individuals.[1,2] Most of the world is currently experiencing a third wave of the disease, and efforts are continuously underway to minimize infectivity, reduce disease severity, and prevent mortality from this novel disease.[3, 4] The challenges associated with this disease include its pattern and rate of infectivity, its severity in the infirm and frail and the lack of knowledge against it.[5]

Accelerated efforts were organized globally to counter the pandemic, the most prominent of which was the development of multiple vaccines within the mind-boggling time frame of a year.[6] The global efforts have resulted in the development of multiple vaccines by multiple countries, which are currently being used to vaccinate populations the world over. This process has also led to the development of the world's first mRNA vaccines against SARS-CoV2, which is a milestone in medicine.[7-9] Inactivated viral particle vaccines have also been developed by different nations and are currently being used for inoculation, one of these is the BBIBP-CorV vaccine being produced by Sinopharm after initial development by the Beijing Institute of Biological Products.[10, 11]

The BBIBP-CorV is a coronavirus vector-based vaccine that contains inactivated coronavirus that retains the spike proteins of the original SARS-CoV2 but is not capable of replicating.[12] This results in an immunogenic response against SARS-CoV2 by producing antibodies against the spike protein on the virus, thus enabling the body to opsonize and neutralize the viral particles. Trials from different countries have reported different efficacies, as original data from China has been limited regarding the BBIBP-CorV vaccine.[6] Vaccine efficacy is difficult to determine particularly in the short term as immunological response may wane over time and adverse events may occur in the long term.[13] Immunogenicity or the antibody response, which can be determined by measuring antibody titres against the particular spike protein, can give us a peek into a type of response which can be expected when exposure to the virus does occur. We present our report on the immunogenicity of the BBIBP-CorV vaccine which is being used in Pakistan to inoculate the masses.

Methodology

A cross-sectional observational study was carried out at HBS General Hospital from March 2021 till May 2021 involving healthcare workers from HBS General Hospital, Rawal General Hospital, Polyclinic Hospital, and PIMS. The non-probability sampling technique was used. Samples were collected from male and female healthcare workers over the age of 18 who had received their second dose of the vaccine at least 2 weeks prior to sample collection and no more than 8 weeks prior to sample collection. The consecutive non-probability sampling duration was March 2021 to May 2021.

Inclusion Criteria: More than 18 years old, male and female healthcare workers, vaccinated individuals who have received the 2 dose BBIBP-CorV vaccine, Individuals who received their 2nd dose of the vaccine at least 2 weeks before sample collection and not more than 8 weeks before sample collection.

Exclusion Criteria: Age less than 18 Years, unvaccinated individuals.

This study was carried out at HBS General Hospital. Ethical approval was obtained from the HBS Medical and Dental College ethical review board. Healthcare workers, who had their Anti-SARS-CoV2 S (Spike Protein antibody) levels checked at least 2 weeks after but not more than 8 weeks after the 2nd dose, were contacted and requested for participation in the study after informed consent. The titer of Anti-SARS-CoV2 S (Spike Protein antibody) was measured in the serum of the participants (which was obtained using centrifugation of blood sample by DLab mixer D2012plus). The titer was measured by Excel Laboratory (using SYSTAAQ Extractor and MIC Amplifier), working in collaboration with Medicine Department of HBS Medical College.

Data was analyzed using Microsoft Excel 2016 and IBM SPSS 22. The mean and standard deviation were calculated for quantitative data like age and titre of antibodies. Frequency and percentages were calculated for analysis of qualitative data like gender, previous COVID-19 infection and Blood group. Stratification was done according to age, gender, titer of antibodies, and the presence or absence of a previous infection.

Results

We included a total of 123 patients in our study. The Male to Female ratio in our study was 1.277:1. Mean age was 42.93±13.234 years. Side effects of the Vaccine were experienced by 42.3% (n=52) of the participants while 21.1% (n=26) of the participants had COVID-19 infection prior to the vaccination. Most of the participants in the study were healthy with no reported comorbidities (86.2% vs 13.8%).

Antibody titers ranged from 0 to 5900, with a mean of 243.26±593.45 U/mL. The Kolmogorov-Smirnov and Shapiro-Wilk tests of normality were applied to the antibody titer and the data was not found to have a normal distribution. The antibody titer was stratified into less than 100, 100-200 and more than 200 U/mL values. Non-parametric tests were applied to check whether there were any differences between the antibody titers based on previous history of COVID-19 infection, gender, and side effects. Post stratification Chi-square tests were also used to compare the frequencies between the above-mentioned groups. The results are demonstrated in table I.

According to the testing methodology, 6.5% of the participants had a negative antibody result (<0.8 U/mL), none of these participants had a previous history of COVID-19 infection. No participants had a borderline result (0.8-1.49 U/mL).

Antibody levels were found to be significantly higher in participants who had a history of previous COVID-19 infection as well as those who reported side effects according to the Mann-Whitney U test ($p < 0.001$ and $p < 0.001$ respectively [asymptotic and exact 2-tailed]).

Table I: showing Mann Whitney U tests performed for the comparison of Antibody titre levels between various groups of interest.

		Mean Antibody Titer (U/mL)	Mean Rank	Sum of Ranks	p-value
Previous COVID-19 Infection	Yes	671.01±1212.55	96.58	2414.5	<0.001
	No	133.01±128.06	52.46	5088.5	
Side Effects	Absent	127.29±139.63	49.81	3486.5	<0.001
	Present	399.36±875.15	77.24	4016.5	
Gender	Male	288.99±774.14	62.59	4319	0.832
	Female	185.66±200.94	61.24	3307	
Age Group	<60 Years	206.4334±303.96	63.62	6870.5	0.171
	≥60 Years	508.86±1500.55	50.37	755.5	

Table II: Table showing the comparison of frequencies of different antibody titre groups using Chi-square test. (n=123)

		Antibody titer range				
		Negative	**1.5-100 U/mL**	**100-200 U/mL**	**More than 200 U/mL**	**p-value**
Previous COVID-19 Infection	Yes	0	1	1	24	<0.001
	No	8	42	14	33	
Side Effects	Absent	8	31	9	23	0.001
	Present	0	12	6	34	
Gender	Male	6	23	7	33	0.594
	Female	2	20	8	24	
Age Group	<60 Years	6	36	13	53	0.342
	≥60 Years	2	7	2	4	

Chi square test was also performed to compare frequencies of presence/absence of side effects with previous history of SARS-CoV-2 infection, although there was a difference (53% of previously infected participants had side effects vs 39% of previously healthy participants, p= 0.179) this did not reach statistical significance.

Stratification was done according to age by dividing <60 years and >60 years old participants. Less than half a quarter of the participants belonged to the >60 years old group (n=15, 12.19%) and although they did have higher mean antibody titre levels (508.86±1500.55 U/mL) as compared to the younger group, this was not statistically significant after the Mann-Whitney U test (p= 0.171).

Discussion

Vaccination is now widely recognized as one of modern medicine's most important tools for stopping epidemics before they spread. In light of the vaccine's importance in countering this public health crisis, familiarity with its potential for triggering allergic responses and other unwanted consequences is mandatory.[14-16] Preclinical trials, where safety and immunogenicity are evaluated in animal models or cell culture, are just one part of the vaccine development process. Phase 1, 2, and 3 vaccine studies are examples of human participants used in clinical trials.[17-20] Vaccines need to be both highly immunogenic and very effective if they are to stop the spread of disease. [7] Review of phase 3 trials conducted in the UAE by Sinopharm indicates an 86% success rate against the COVID-19 virus. and 100% effective in preventing moderate and severe disease.[21] Vaccination efforts currently underway all over the world are the most important weapon in our arsenal against the COVID-19 pandemic. A number of different vaccines have been developed in different areas of the world. These include the breakthrough mRNA vaccines currently being used mostly in the western developed world, as well as the traditional viral vector and inactivated viral particle vaccines currently being used in most of the developing world. The BBIBP-CorV Vaccine or Sinopharm vaccine was one of the first vaccines which were rolled out to the developing world. It is an inactivated SARS-CoV-2 vaccine developed by the Beijing institute of biological products and was donated to many developing countries by China. This is one of the most frequently used vaccines in Pakistan to inoculate the population against SARS-CoV-2. We measured the neutralizing anti spike protein (S) antibody levels in the healthcare workers at least 2 weeks post-inoculation but not more than 8 weeks post-inoculation.[22] Our titre data was not normally distributed, and non-parametric tests were applied to compare the titres between different groups of interest.

As per the testing methodology 8 (6.5%) of the participants had negative antibody results with levels lower than 0.8 U/mL. None of these participants had history of previous SARS-CoV-2 infection or any side effects of the vaccine. Out of the participants who had a

negative result, 6 were older than 60 years of age. Previous history of SARS-CoV-2 infection was reported by 26 (21.1%) of the participants. These participants were found to have significantly higher levels of antibody titres as compared to participants who did not have previous history of SARS-CoV-2 infection.

This was expected as the vaccine had boosted their antibody response. The mean antibody titre in this group of participants was 671.01±1212.55 U/mL with a maximum level of 5900 U/mL. A review of published literature showed that this particular group was not included in any of the different vaccine trials due to the pre-existing immunity against the disease which precluded the calculation of efficacy of the vaccine candidates. An interesting finding in our study was that the participants who reported side effects to the vaccine (n=52, 42.2%) had a significantly higher antibody titre as compared to participants that did not report any side effects. The mean antibody level in the side effect group was 399.36±875.15 U/mL and the Mann-Whiney U test had a significance of <0.001. We may be able to say from this result that a higher antibody titre is related to the presence of side effects of the BBIBP-CorV vaccine. Chi square test post-stratification of the antibody titre levels also showed that significantly more participants were a part of the >200 U/mL group as compared to the participants who did not experience any side effects.

Conclusion

The BBIBP-CorV vaccine elicited immunogenicity leading to detectable Anti Spike protein S antibody levels in 93.5% of the patients in our study, with greater levels in patients previously exposed to SARS-CoV2. However, 6.5% of the study participants did not have a detectable level of the antibody. Further research is required to elucidate in detail the levels of protection achieved by the vaccine.

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