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Comparison of Pre and Post Vaccinated Covid-19 Antibody Titers in General Population

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Abstract

Objective: The aims and objectives of this study to examine the general population one year later following immunization for changes in anti-SARS-CoV-2 IgG levels.
Methodology: The study enrolled 18,610 individuals, including rural and urban areas. The quantities of IgG antibodies were determined using an ELISA.
Results: At 5–8 months following complete immunization, both vaccines produced comparable amounts of anti-SARS-CoV-2 IgG. On the other hand, BBIBP-CorV had a much lower IgG concentration. Anti-SARS-CoV-2 IgG levels in a large cohort of volunteers increased nine months after vaccination, indicating asymptomatic infection. Anti-SARS-CoV-2 IgG antibody levels were significantly higher following the booster dose than following the second dose. Antibodies began to build approximately five days after the booster dosage injection and peaked around the fourteenth day.
Conclusion: Cut-off dates for the effectiveness of mRNA and vector vaccines appear to be 8–9 months and 5–6 months following vaccination, respectively. With the potential to have a significant impact on the virus's ongoing transmission, providing a booster dose was a brilliant idea.
Key words: SARS-CoV-2, IgG antibody, mRNA.

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Introduction

Coronavirus disease 2019 (COVID-19) is caused by the SARS-CoV-2 virus, which has been responsible for the infection of about 440 million people worldwide. COVID-19 was first detected in Pakistan on March 4, 2020. Over 5.69 million cases have been reported since then, resulting in approximately 112,000 deaths.[1]

On December 27, 2020, the so-called National Vaccination Program began immunizing healthcare staff in Pakistan against COVID-19, and the program was gradually expanded to include the general population as the population grew older. Vaccinations began in June 2021 for children aged 12-17 years, and in December 2021 for children aged 5-11 years. After nearly a year, more than 53 million people have received anti-COVID-19 immunization. Pakistan's population is predicted to get vaccinated at a rate of 58.5 percent. Almost 30% of those vaccinated had a booster dosage, which is the third and final injection.

Prophylactic immunization appears to be the most effective strategy for combating the SARS-CoV-2 pandemic, as it reduces the risk of severe COVID-19, the number of hospitalizations and fatalities from the disease, and brings the pandemic closer to an end.[2,3] In Pakistan, four types of anti-SARS-CoV-2 vaccinations have been delivered. For instance, both the Pfizer/BioNTech, Moderna, AstraZeneca and Sinopharm vaccine employ mRNA technology. The vaccine's nucleoside-modified messenger RNA is encased in lipid nanoparticles to allow non-replicating RNA to enter host cells and transiently express the SARS-CoV-2 virus S antigen. For individuals above the age of 12, Pfizer medication is safe to ingest with a 21-day interval between dosages. It was approved in mid-September 2021 for adults over the age of 50 and healthcare providers to receive the third dosage of the

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immunization. For seven days to six months following the second dosage, this vaccine is 94% effective at preventing illness., it was 100 percent effective at preventing serious sickness and death.[4] mRNA1273 (Moderna) vaccinations commenced in Pakistan on January 20th, 2021. Adults over the age of 18 should repeat the dose 28 days following the initial dose. When a vaccination is given a second time, it is 95% effective in preventing disease and 100% effective in preventing severe disease.[5] The following two vector vaccines are ChAdOx1 nCoV-2019 (AstraZeneca) and BBIBP-CorV (Sinopharm). A single recombinant chimp adenoviral vector encodes the SARS-CoV-2 virus S glycoprotein in ChAdOx1 nCoV2019, a monovalent vaccine. As of February 2021, this vaccine can be administered to people aged at least 18 years in Pakistan with a 28 to 84-day interval between doses. When compared to mRNA vaccines, the effectiveness of ChAdOx1 nCoV-2019 is already significantly lower. As a result, it should theoretically be able to protect you from all sorts of major illness.[6] Sinopharm vaccine is the least effective of the vaccinations. COVID-19 is 66%–72% efficient in preventing infection and 85% effective at preventing the disease's most severe manifestations.[7] All vaccinations lose their capacity to protect against infection after six months of vaccination. BNT162b2, mRNA-1273, and BBIBP-CorV. each have 45%, 58%, and 13%. While these levels remain high, protection against severe COVID-19 and death has decreased significantly after this time period: 70% for BNT162b2, 76% for mRNA-1273, and 52% for BBIBP-CorV.[8]

As a consequence of this investigation, the time interval between complete vaccination and attainment of maximum immunological parameters, which gives the best protection against sickness, was determined. However, research is being conducted to ascertain the duration of this protective period. Despite the vaccine's outstanding success, additional research into how varied groups respond to it is required. Only with constant post-vaccination monitoring can the duration of protection and the time of booster doses be identified. Whether or not a long-term protective effect is possible is also a significant subject. As a result, long-term responses must be investigated. The research team for this project is made up of employees from medical institutes. As the first cohort to receive a booster injection against SARS-CoV-2 infection, the vast majority of this cohort received vaccination in so-called "group 0." As such, they provide an ideal resource for examining the changes in anti-SARS-CoV-2 IgG levels post vaccination, as well as their stability over time. The purpose of this study is to determine the dynamics and durability of anti-SARS-CoV-2 IgG levels 1–12 months and 1–3 months after receiving the first and second doses of immunization with the four vaccines now available in Pakistan (i.e., BNT162b2, mRNA-1273, ChAdOx1 nCoV-2019 and BBIBP-CorV).

Material and Methods

We have effort to study a specific post-vaccination response measure. To combat the detrimental effects of COVID-19, preventive and prophylactic measures have been developed. The program's implementation began on March 1, 2020, and will last through June 30, 2022. Our study comprises of general entities in random population. The current analysis incorporates data from diagnostic tests completed through the end of 2021. Between June and December 2021, 18,838 personnel were tested for antibodies as a result of these operations. The ability to analyse the data collected, on which this study is based, is another critical skill for scientific research.

Several patients were omitted due to a lack of data, most commonly due to missing vaccination dates or SARS-CoV-2 sickness. There were 18,610 individuals in the research group, including physicians, nurses, midwives, paramedics, and laboratory diagnosticians. Women made up 81.3 percent of participation, while men made up 18.7 percent, highlighting the vast gender disparity (Table I). Adults aged 46 to 55 made up 33.3 percent of the population, while those above the age of 66 made up 3.9 percent. At various stages throughout the experiment, subjects received four separate COVID-19 vaccinations. Between September and December, 3191 patients received the third dose of the Pfizer/BioNTech vaccine after receiving the ChAdOx1 nCoV-2019 immunization (5.2 percent of participants; Table I).

We determined the levels of IgG anti-SARS-CoV-2 using an enzyme-linked immunosorbent assay with the automatic analyzer EUROIMMUN Analyzer I-2P and the Anti-SARS-CoV-2 QuantiVac ELISA kit in accordance with the manufacturer's instructions and a detailed description of the methodology from our previous research. The investigations used plates coated with recombinant SARS-CoV-2 S1 domain (containing RBD) generated in the human HEK293 cell line (ATCC).

Results

Table I: Frequency Distribution of Age, Gender, Covid status and Vaccination Type							
		Total	Unvaccinated	BNT162b2	mRNA-1273	ChAdOx1 nCoV-2019	BBIBP-CorV
Age (y)	Under 35 36–45 46–55	3337 (17.9%) 3720 (20.0%) 6201 (33.3%)	383 (24.4%) 354 (22.5%) 459 (29.2%)	2539 (16.5%) 3020 (19.6%) 5247 (34.0%)	222 (22.8%) 210 (21.6%) 291 (29.9%)	106 (37.9%) 73 (26.1%) 59 (21.1%)	87 (23.6%) 63 (17.1%) 145 (39.3%)
	56–65	4622 (24.8%)	341 (21.7%)	3960 (25.7%)	222 (22.8%)	33 (11.8%)	66 (17.9%)
	66+	729 (3.9%)	33 (2.1%)	650 (4.2%)	29 (3.0%)	9 (3.2%)	8 (2.2%)
Gender	Female Male	15,133 (81.3%) 3477 (18.7%)	1308 (83.3%) 262 (16.7%)	12527 (81.3%) 2890 (18.7%)	784 (80.5%) 190 (19.5%)	225 (80.4%) 55 (19.6%)	289 (78.3%) 80 (21.7%)
COVID-19 status	No infection Before vaccination After vaccination	12,397 (66.6%) 6188 (33.3%) 575 (3.1%)	941 (60.1%) 621 (39.6%) 0 (0.0%)	10550 (68.4%) 4848 (31.4%) 554 (3.6%)	553 (56.8%) 421 (43.2%) 13 (1.3%)	156 (55.7%) 123 (43.9%) 0 (0.0%)	194 (52.6%) 175 (47.4%) 8 (2.2%)
	Twice	19 (0.1%)	5 (0.3%)	14 (0.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Potential	266 (1.4%)	15 (1.0%)	221 (1.4%)	16 (1.6%)	11 (3.9%)	3 (0.8%)

Table II: Antibody Concentration in Study Population							
Group	Minimum	1st Quartile	Median	Mean	3rd Quartile	Maximum	SD
Overall (N = 941)	3.2	3.2	13.96	105.42	94.75	7680	488.80
No antibodies (≤35.2)	3.2	3.2	3.2	6.959	5.71	35.09	7.44
Antibodies detected (>35.2)	35.87	69.01	119.30	247.62	230.93	7680	741.95

Table III: Comparison of antibody levels among vaccinated healthy individuals								
Group		Minimum	1st Quartile	Median	Mean	3rd Quartile	Maximum	SD
Healthy vaccinated (2 dose) more than 6 months before the antibody measurement	Overall (*N* = 6620)	3.2	101.4	185.2	424.6	354.1	7730	911.40
	Low antibody level (≤2500)	3.2	95.85	169.85	275.08	306.30	2473.60	337.91
	High antibody level (>2500)	2539	3763	4412	5062	7159	7730	1793.01
Vaccinated (3 dose), overall		3.2	1490	2405.80	3007.80	3971.6	19,200	2161.04

Table IV: IgG Levels for Pfizer/BioNTech Vaccinated Individuals				
Factors and Levels	BNT162b2		mRNA-1273	
	Mean IgG concentration	**95% CI**	**Mean IgG concentration**	**95% CI**
≤3 months	1772.822 (948)	(1678.493, 1867.151)	2170.207 (121)	(1573.818, 2766.596)
3–6 months	601.301 (3461)	(582.563, 620.039)	1050.766 (107)	(889.980, 1211.552)
6–9 months	626.441 (7909)	(607.381, 645.500)	1224.907 (34)	(727.943, 1721.871)
9+ months	2384.526 (1937)	(2274.893, 2494.159)	-	-
≤3 months, no	1517.258 (512)	(1401.604, 1632.913)	2149.050 (72)	(891.700, 3406.400)
≤3 months, yes	2034.188 (436)	(1880.238, 2188.138)	2240.479 (49)	(1873.151, 2607.806)
3–6 months, no	399.911 (2109)	(384.389, 415.432)	1065.031 (55)	(796.358, 1333.704)
3–6 months, yes	803.615 (1352)	(769.536, 837.694)	1041.315 (52)	(860.521, 1222.110)
6–9 months, no	407.1315 (5546)	(393.041, 421.222)	1044.596 (23)	(617.441, 1471.751)
6–9 months, yes	845.875 (2363)	(810.85, 880.900)	1445.786 (11)	(555.032, 2336.539)
9+ months, no	2537.310 (1520)	(2431.067, 2643.552)	-	-
9+ months, yes	2237.735 (417)	(2046.920, 2428.549)	-	-

Among the 18,610 participants, 1565 individuals were unvaccinated (8.41 percent). 621 was acquired via SARS-CoV-2 (based on a positive qPCR test). Fifteen patients were found to have the virus, five of whom had re-infected.

This study enrolled 941 volunteers who were not vaccinated or sick. 385 respondents reported antibody concentrations more than 35.2 BAU/mL. (cut-off value of the positive result). We were unable to reject the null hypothesis that 41% of COVID-19-infected patients recovered using the t-test. The 95 percent confidence intervals for the percentage of people who survived SARS who were not vaccinated were 37.77 percent and 44.06 percent. Table II summarizes the antibody concentrations.

Patients who got two doses of the vaccine and were completely immunized (N = 13,648) and had not previously declared a COVID-19 infection had their antibody levels evaluated at least six months after the previous dose (Table III). 190 patients in this group had antibody levels greater than 2500. According to the t-test, 2.9 percent of those who received the SARS-CoV-2 vaccine early and had no symptoms consistent with COVID-19 infection were actually infected.

Table V: IgG Levels for AstraZeneca and Pfizer/BioNTech Vaccinated Individuals				
Factors and Levels	ChAdOx1 nCoV-2019		BBIBP-CorV	
	Mean IgG concentration	**95% CI**	**Mean IgG concentration**	**95% CI**
≤2 months	702.293 (245)	(631.245, 773.340)	1337.550 (172)	(1090.454, 1584.645)
2–4 months	413.318 (336)	(373.365, 453.27)	688.845 (131)	(547.739, 829.95)
4+ months	519.249 (321)	(455.447, 583.051)	1058.729 (58)	(784.584, 1332.875)
≤2 months, no	473.535 (123)		891.668 (92)	(612.647, 1170.689)
≤2 months, yes	938.1125 (122)	(807.835, 1068.390)	1791.968 (80)	(1402.612, 2181.325)
2–4 months, no	269.658 (188)	(238.669, 300.647)	704.624 (70)	(492.279, 916.969)
2–4 months, yes	556.898 (148)	(483.554, 630.242)	672.644 (61)	(488.824, 856.464)
4+ months, no	409.152 (196)	(328.539, 489.765)	1293.385 (30)	(810.096, 1776.675)
4+ months, yes	634.559 (125)	(536.503, 732.615)	842.969 (28)	(596.795, 1089.142)

15,237 participants received two or three doses of the Pfizer/BioNTech vaccine. 982 outliers who surpassed the top quantile by three interquartile ranges were excluded from groups based on time since full immunization (3 months, 3–6 months, 6–9 months, and 9+ months) and prior COVID-19 infection (no, yes) (Table IV). The data set was complete after 14,255 observations.

AstraZeneca administered the vaccination to a total of 959 patients. In June, AstraZeneca vaccines were suspended in Pakistan, with only the second dosage administered to patients who had previously begun the series. As their third dose, participants in this group got Pfizer/BioNTech. Prior COVID-19 infection (no, yes) and time since full immunization (two months, two–four months, or four months or more) were used to eliminate 57 outliers who were three interquartile ranges over the highest quantile (Table V). Finally, the dataset contained 902 observations.

Discussion

The pandemic of the COVID-19 virus has elevated vaccines to a key hope for humanity, and they are currently being deployed in large-scale global vaccination campaigns. Despite unresolved issues regarding vaccination duration, transmission prevention, and protection against emerging viral variations, COVID-19 vaccines may be an important weapon in reducing SARS-CoV-2 infection, severe sickness, and mortality, as well as more broadly in combating a pandemic. Anti-SARS-CoV-2 IgG antibodies directed against the coronavirus S protein were evaluated in response to injection with four vaccinations that are already available in Poland: BNT162b2, mRNA-1273, ChAdOx1, nCoV-2019, and BBIBP-CorV. The statistics reported here are based on measures collected between one month and one year following vaccination. While the entire viral spike protein is employed as an antigen in all currently available Phase 3 vaccines, the way by which it is presented to the immune system varies. Purity and the presence of other chemicals capable of altering the immune response and causing adverse effects are also distinct.[9]

According to preliminary findings, persons who received mRNA shots had much greater antibody titers than those who received vector vaccinations four months following full immunization. Tretyn and Szczepanik's conclusions, as well as those of other studies, corroborate these findings.[13,15–17] Additionally, it has been demonstrated that adenovirus-based vaccines have limitations in that they induce robust T-cell responses but produce fewer neutralizing antibodies.[10–12] Because a cellular response and immunological memory protect against severe disease and hospitalization, vaccine-induced humoral and cellular responses protect against re-infection and illness symptoms. A booster dose is required to protect against SARS-CoV-2 infection, as vector vaccination results in a diminished humoral response.[14] This has resulted in the suggestion of a booster dose of mRNA immunization for individuals who have received vector shots.

Recently, it was discovered that heterologous vaccine administration, as opposed to homologous vaccine injection, elicits the highest immune response.[18] When mRNA-1273 was compared to other mRNA vaccines, anti-SARS-CoV-2 antibody production was significantly higher in healthy individuals prior to immunization and in those with COVID-19. Numerous investigations have demonstrated MRNA-1273's heightened immunogenicity and increased antibody response to BNT162b2.[19-21]

Immune responses to two mRNA-containing vaccinations were assessed in people with and without antibodies. The results indicate that the mRNA-1327 vaccine causes considerably larger levels of S-RBD total antibodies (3.5-fold; $p < 0.001$), S-RBD IgG (2-fold; $p < 0.01$), and S-IgA (2.1-fold, $p < 0.001$) in the healthy vaccinated group than the BNT162b2 vaccine. Individuals who have previously been infected produce significantly more S-RBD IgG ($p < 0.05$), but not significantly more than the healthy-

BNT162b2 group.[25] Richards and colleagues[25] also discovered a reduced level of IgG antibodies against SARS-CoV-2 RBD following BNT162b2 injection compared to mRNA-1273 (geometric means, pre-boost blood draw: 19.1 g/mL vs. 5.9 and post-boost blood draw: 68.5 g vs. 45.9 g/mL).[22-23]

Because Pfizer and Moderna manufacture their vaccines differently, these findings can be explained by the fact that the RNA carriers, LNP, and minor product-specific RNA sequence variations differ somewhat between the two vaccines.[14] On the other hand, MRNA-1273 required 100 grammes of RNA to function, whereas the BNT162b2 vaccination required only 30 grammes. There is a slight delay between the second and third vaccine doses with mRNA-1273, which should be considered. When it comes to vaccine immunological response, it appears as though delaying the second dosage is beneficial.[26]

When SARS-CoV-2 IgG levels are summarized over time following injection with four distinct vaccines, the antibodies produced in response to the mRNA vaccine, particularly the Comirnaty, demonstrate significantly more dynamics of change over time.[27] Erice et al. examined antibody levels 1.5 and 3 months after two doses of the BNT162b2 vaccine. They had median anti-RBD antibody concentrations of 3952 (AU/mL), confirming the considerable range of antibody levels throughout time. Levin and colleagues discovered that the Pfizer vaccine had a considerable incidence of antibody change six months after the second immunization.[28-30] Brisotto et al. found that the level of spike RBD-specific antibodies altered dramatically four months after the second injection of mRNA-1237.[31] Immunization with the ChAdOx1 nCoV-2019 vector resulted in higher durable antibodies against the SARS-CoV-2 S protein. Numerous scientists have reported similar findings. Mishra et al. examined anti-SARS-CoV-2 antibody titers one month after the Oxford/AstraZeneca vaccine was provided (Round 1), as well as one and six months after the second dose was trimmed (Rounds 2 and 3). In Round 1, geometric mean IgG titers were 138.01 BAU/mL, 176.48 BAU/mL in Round 2, and 112.95 BAU/mL in Round 3.[32]

Anti-SARS-CoV2 IgG titers in vaccinated convalescents are approximately 2–10 times higher than in seronegative vaccinates at the same time. There are discrepancies between pre-vaccination seronegative and seropositive individuals in the case of the ChAdOx1 nCoV-2019 vector vaccine, but they are not as significant as they are for other vaccinations. Anti-SARS-CoV-2 IgG antibodies can persist for up to 13 months in up to 80% of individuals who were not immunized following COVID-19 infection.[33–35] The reduction in IgG and neutralizing antibodies was much lower in those who were previously infected with COVID-19 than in those who were newly vaccinated.[36]

Additionally, Eyre et al. measured anti-SARS-CoV-2 antibody levels in patients who had previously been infected with the virus. The median antibody response was 14,604 AU/mL >21 days after the initial Pfizer/BioNTech infection, compared to 1028 AU/mL in the absence of previous infection, demonstrating a much higher quantitative antibody response. Post-first dose values in Oxford/AstraZeneca vaccination recipients with or without prior infection were lower—10,095 and 435 AU/mL, respectively—than in Pfizer/BioNTech vaccination recipients. After the second Pfizer vaccination, the antibody response in people who had not previously been infected was equivalent to those following prior infection followed by one vaccine dosage at >21 days after the second vaccination, 10,058 AU/mL.[37] Additionally, it was shown that those who had COVID-19 prior to immunization had considerably higher levels of anti-SARS-CoV-2 antibodies following vaccination with BNT162b2 than seronegative individuals.[38]

Conclusion

Immunization with four vaccines available in Pakistan between 1 and 12 months after injection allowed us to study the kinetics and persistence of antibodies against the SARS-CoV-2 S1 subunit in response to that vaccination. The IgG levels were identical six months following vaccination with the BNT162b2, mRNA-1327, and ChAdOx1 nCoV-2019 vaccines despite the higher immune response elicited by the mRNA vaccines. It was demonstrated that the BBIBP-CorV vaccine produced the least immunological response. With mRNA vaccines, it appears that protection begins 8–9 months after vaccination, however with vector vaccines, protection begins 5–6 months after vaccination. SARS-CoV-2 apparently infected a significant number of persons with no symptoms, as demonstrated by the large number of cases. After careful deliberation, the decision to introduce an additional dose in September 2021 was justified, and it has enormous potential to restrict the spread of the virus. This hypothesis is confirmed by the low infection rate found following full vaccination. Because many persons who had been vaccinated six months before the test

showed elevated antibody titers, it's plausible that these people were infected with SARS-CoV-2 but had no symptoms. Even six to twelve months after a thorough immunization, the immunizations are still able to protect against serious disease. We are more willing to study whether or not referring patients for essential booster vaccines would be better served by integrating serological testing in the process. Since the third dose, numerous persons have generated stronger antibody titers than those who only had the latent vaccination.

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