



## Comparison of Antibody Levels Produced by Pfizer, AstraZeneca, and Sinopharm Vaccination in COVID-19 Patients in Erbil City-Iraq

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### ARTICLE INFO

#### Original paper

#### Article history:

Received: January 19, 2023

Accepted: March 13, 2023

Published: March 31, 2023

#### Keywords:

COVID-19, Anti-spike-specific antibodies, ELISA, Pfizer, AstraZeneca, and Sinopharm vaccine

### ABSTRACT

In this study, early adverse impacts that emerged after vaccination with each dose of these vaccines were compared with previously infected participants. Ant-SARS-CoV-2 spike-specific IgG and IgA antibodies produced by these three vaccines have been assessed using the ELISA method at different time periods; including pre-vaccination, and post-vaccination with Pfizer-BioNTech, AstraZeneca, and Sinopharm vaccine. Overall, 150 previously infected cases were studied, 50 cases received the Pfizer vaccine, 50 cases received the AstraZeneca vaccine, and 50 cases received the Sinopharm vaccine. The findings showed that a higher number of vaccinated participants with AstraZeneca and Pfizer vaccines had tiredness/fatigue/lethargy, headache, fever, and soreness in the arm at the first shot, but milder adverse effects, such as headaches, fever, and soreness in the arm, were detected in the data on the Sinopharm vaccine's adverse impacts. At the second dose, a lower number of vaccinated cases with AstraZeneca, and Pfizer vaccines reported higher frequencies of the side effects. However, the results showed that the level of anti-spike-specific IgG and IgA antibodies produced by vaccinated patients with the Pfizer vaccine increased compared to those who were vaccinated with AstraZeneca and Sinopharm vaccine from 25 days after the first dose. From 30 days after the second dose, the IgG and IgA antibodies were significantly boosted in 97% of vaccinated patients with the Pfizer vaccine compared to 92% of those who were vaccinated with AstraZeneca vaccines, and 60% of those who were vaccinated with Sinopharm. In conclusion, these results confirmed that two doses of the Pfizer, and AstraZeneca vaccines induce a higher response of IgG and IgA antibodies than that induced by Sinopharm vaccines.

Doi: <http://dx.doi.org/10.14715/cmb/2023.69.3.14>

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### Introduction

Coronavirus disease 19 (COVID-19) is a non-eradicated disease that is caused by a virus called Severe acute respiratory syndrome 2 (SARS-CoV-2) (1). Since the SARS-CoV-2 emergence, Scientific research found that SARS-CoV-2 has different club-like spike proteins protruding from its surface. These spikes latch onto cells in the body by binding to receptors (known as ACE2 receptors) on the cell surface, once attached the virus fuses with the cell and the viral genetic material passes into the cell. Where it is copied creating more viral particles and causing more infection (2-4). Scientific research has been underway to combat the COVID-19 pandemic in different ways. Firstly, medicines may treat the infection by stopping the virus from replicating and by suppressing the body's overactive immune response or protecting it from serious complications such as organ failure (5). Secondly, Novel coronavirus-neutralizing antibodies that can bind to the virus and stop it from entering cells as a possible treatment to prevent or lessen the impact of the current COVID-19 disease (6). Lastly, a vaccine has been developed as a preventative approach. All COVID-19 vaccines are aimed to produce immunity to the SARS-CoV-2 virus by stimulating an immune response to an antigen. Usually, the characteristic spike protein is found on the surface of the virus. There have been multiple approaches to vaccine development to prime the body's immune response to

the current COVID-19 pandemic (7, 8). Using weakened viruses or viral proteins or creating a viral vector with a specific viral genetic code or using specific viral genetic code either DNA or RNA directly. Viral vectors are engineered to prevent them from being able to replicate and cause disease but can carry a specific genetic material to deliver inside a cell. The vaccine is introduced into the body through injection encompassing the genetic material of the SARS-CoV-2 spike protein (9). The vaccine Pfizer-BioNTech (carries spike mRNA) and AstraZeneca (a viral vector that carries spike mRNA) has a similar approach which penetrates the cell membrane and fuses with the cell. Inside the cell, the genetic material is processed to form the spike protein which is presented on the cell surface. B-cell and T-cell lymphocytes recognize the spike protein as foreign and start to multiply to form an army of identical B-cells and T-cells. The B-cells release antibodies into the circulation to bind to the virus and neutralize it. The T-cells also help activate B-cells or eliminate infected cells. Both B-cells and T-cells form memory cells that are ready when the body is exposed to the virus at a later stage. Upon exposure to the live SARS-CoV-2, the immune response is primed to neutralize the virus and reduce the impact of the disease (10, 11). The Pfizer-BioNTech and Oxford-AstraZeneca vaccines were proven to be extremely successful in phase III clinical studies when used in a second dose regimen with a goal interval of three and four weeks, respectively. According to a reanalysis of the

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Pfizer-BioNTech trial results, a single dose of this vaccine shows a 92.6 percent efficacy in the early post-vaccination interval. According to the results of the Oxford-AstraZeneca experiment, longer dose intervals may provide better protection. According to a new study, Pfizer's COVID-19 vaccine makes more than double the antibodies detected from AstraZeneca's COVID-19 vaccine. The research compared the antibody levels produced against the spike protein of SARS-CoV-2. Among those who had not been previously infected, the people who got the Pfizer vaccine averaged 2,301 units per milliliter, as compared with those who were vaccinated with the AstraZeneca vaccine, who averaged 1,130 units per milliliter (11).

The BBIBP-CorV (Sinopharm) vaccine, on the other hand, is a traditional vaccine achieved by modifying the virus to weaken or disable it. So that when introduced to the body, an immune response can be made to the antigen without virus-causing disease. When the immune system comes into contact with the weakened virus, its defenses, such as antibodies and T-cells attack the virus or infected cells (12, 13). Multiple copies of the SARS-CoV-2 virus are produced in these cells, which are subsequently treated with beta-propiolactone, which deactivates the virus by binding to its genes. This vaccine was found to be 79.34 % effective in phase III clinical studies carried out in Egypt, Morocco, Pakistan, Bahrain, Peru, Argentina, and the United Arab Emirates (UAE). The vaccine was approved for emergency use by WHO in May after clinical studies. Two doses of vaccine must be given three to four weeks apart, according to WHO recommendations. Milder adverse effects, such as headaches, fever, and soreness at the injection site, are listed in the data on the vaccine's side effects (14).

In the present study, the dynamics of the IgG and IgA response in the previously infected cases was aimed. The adverse symptoms of vaccination with the Pfizer-BioNTech, Oxford-AstraZeneca, and Sinopharm vaccine were determined in people who were previously infected with COVID-19. The effectiveness and efficacy of vaccination with the Pfizer-BioNTech, Oxford-AstraZeneca, and BBIBP-CorV vaccine on the anti-SARS-CoV-2 spike-specific IgG and IgA antibodies produced by the immune system was assessed.

## Materials and Methods

### Sample collection

The dynamics of the IgG and IgA response in the previously infected cases was illustrated in Figure 1. Total of 150 Kurdish individuals were monitored and divided into three groups; 50 previously infected cases who received the Pfizer COVID-19 vaccine, 50 previously infected cases who received the AstraZeneca COVID-19 vaccine, and 50 others who received BBIBP-CorV. The cases were followed up at Nawroze hospital center. All participants were already confirmed by Real-Time Polymerase Chain Reaction (RT-PCR) to make sure that they had previously been infected. In the present study, the full Pfizer, AstraZeneca, and Sinopharm vaccination program and then were tracked for all three measurements: one day before vaccination (pre-vaccination), 25 days after the first shot, and 30 days following the second shot. All the cases had no other disease or pregnancy during testing. Table 1 showed the demographic features of the participant cases.

### Blood sampling

Blood samples were withdrawn by syringe from the tested group and put in blood clot activator tubes (Cat. No. 302315, Germany) during the evening hours. Then, the blood samples were immediately centrifuged using Eppendorf MiniSpin (Cat. No. 5452, Canada) at 2000 rpm

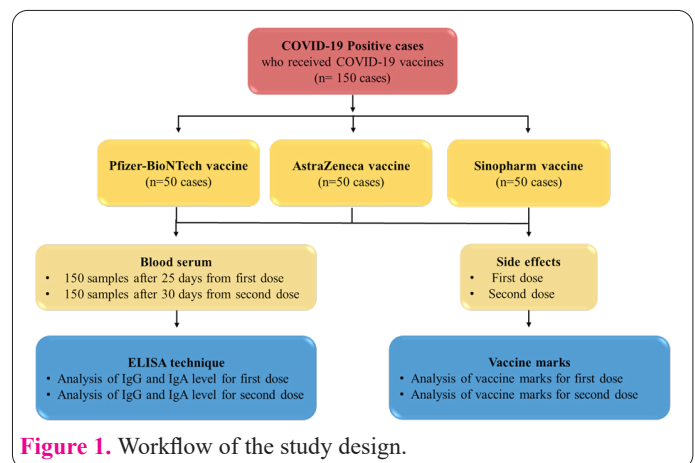


Figure 1. Workflow of the study design.

Table 1. Demographic features of infected cases vaccinated by Pfizer and AstraZeneca vaccine.

Demographic	Pfizer-vaccinated case (%)	AstraZeneca-vaccinated cases (%)	Sinopharm-vaccinated cases (%)
<b>Sex</b>			
Male	40(80)	45(90)	6(12)
Female	10(20)	5(10)	44(88)
<b>Age</b>			
<50	40(80)	35(70)	16(22)
≥50	10(20)	15(30)	34(68)
<b>BMI</b>			
≤20	21 (42)	25(50)	21(42)
20-25	18 (36)	13(26)	15(30)
≥25	11 (22)	12(24)	14(28)

BMI; Body mass index.

for 5 minutes at room temperature within 2 hours of blood collection. The serum samples were stored at -20°C in the refrigerator (Cat. No. 2325LG, Japan) of the private laboratory of Bio and Pharma for IgG and IgA analysis.

### ELISA method

Bio Tek instrument (Reference No. 800TS, USA) was used to measure the serum levels of the IgG and IgA antibodies. ELISA Kits of IgG (PT-SARS-CoV-2 IgG 96, Eurofins technology, Hungary) and IgA (VIROTECH SARS-CoV-2 IgA 96, Eurofins technology, Hungary) were used to analyze the serum levels of the antibody of IgG and IgA, respectively. The kits of Anti-SARS-Cov-2 antibodies are commercially available and have been authorized by Kurdistan Region Government (KRG). Previously, these kits have been authorized by the European Medicines Agency (EMA). The procedure was carried out according to the manufacturer's instructions. To sum up, the kits include ELISA plates coated with the SARS-CoV-2 spike protein's recombinant S1 domain, which was generated in the human cell line HEK 293. All of the reagents needed to generate the ELISA are included in the kit, including: Calibrator (human IgG, and IgA, respectively). The following cutoff index (COI) is recommended by the manufacturer: negative ratio  $\leq 1.1$  and positive ratio  $\geq 1.1$ . As designated by the supplier of IgG and IgA kit, the results are given as indices. Variables is presented as the mean  $\pm$  standard deviation (SD) of each data when suitable.

### Statistical Analysis

Data were then analyzed by GraphPad Prism 8.0 (GraphPad Software). For all of the groups that were examined, the correlation between the first and second dose of each vaccine was determined, taking into account of *P*value.

### Genomic analysis

In this study, 100 genomic sequences of SARS-CoV2 strains were collected from the National Center of Biotechnology Information (NCBI) database to know whether the Pfizer, AstraZeneca and Sinopharm vaccine are safe and effective among the population in the Kurdistan region of Iraq. The phylogenetic tree was constructed to show the relationship between SARS-CoV-2 strains used to generate these vaccines and strains identified in the Kurdistan region of Iraq.

## Results

### Parameters of vaccination

Three parameters were tested for the participant groups, Prior to immunization (pre-vaccination), 25 days

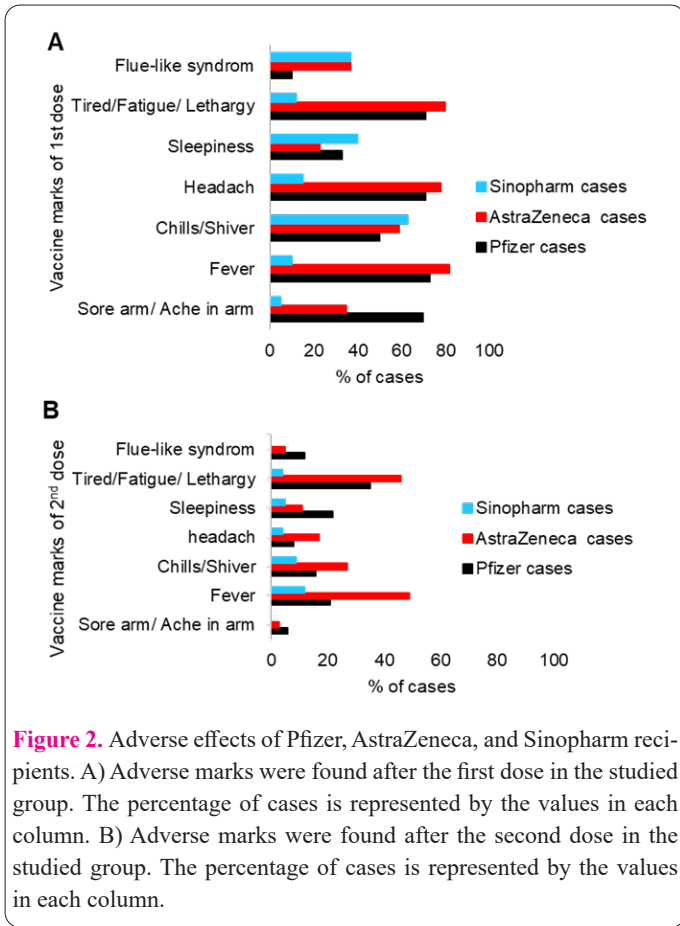
after the first shot, and 30 days after the second dose. The levels of IgG and IgA antibodies were measured. Prior to vaccination, both specific IgG and IgA levels were considerably high due to the infection with COVID-19 disease (Table 2). The SD of the mean was high in infected participants and the higher SD of value registered for antibody levels in infected participants indicates that the antibody's responses to infection are more variable due to a specific/individual immune response and, as a result, due to a variety of factors. Because of these statistically significant differences, the post-vaccination dynamics for previously infected cases are shown separately. Prior to vaccination, IgG or IgA values were not connected with age or gender, regardless of whether you were infected or not. IgG and IgA levels were moderately higher in the Pfizer recipients, as compared to AstraZeneca and Sinopharm recipients. Table 2 showed that IgG and IgA levels produced by first and second doses of the Pfizer and AstraZeneca vaccine were higher noticeably than the antibodies produced by both shots of the BBIBP-CorV vaccine.

### Adverse effects upon Pfizer, AstraZeneca, Sinopharm vaccination

Although three groups are nearly equally likely to claim the worst adverse effect they experienced, persons who received the AstraZeneca vaccine are more likely to report side effects (24 percent versus 10 percent). The presence of any side effects was reported for each recipient after the first and second shots from the COVID-19 immunization. Figure 2 shows the effective marks and the proportion of these adverse effects in both groups for the first shot (A) and the second shot (B). Furthermore, there was no correlation between the occurrence of negative effects and age or gender. Fever soreness at the injection site, tiredness/fatigue/lethargy and headache were the most common adverse effects in this study. AstraZeneca vaccine recipients in the first dose are slightly more likely to report severe fever (82%), sore arm/ache of the arm (83%), tired/fatigue/lethargy (80%), and headache (78%). In each case, this was 5-10 percentage points higher than among Pfizer vaccine recipients; while, these side effects remained the most common marks for the second shot of AstraZeneca and Pfizer recipients, as compared to BBIBP-CorV recipients. When it comes to the specific adverse symptoms experienced. those who received the first dose of the AstraZeneca vaccine are substantially less likely to report suffering from a minor sore/aching arm from the injection (35%, compared to 70% of Pfizer recipients); whereas, this side effect was significantly lower from those who received the second shot of AstraZeneca vaccine (18%) than those who received the second shot of Pfizer vaccine

**Table 2.** Serum IgG and IgA before and after Pfizer and AstraZeneca vaccine.

Index means	Pfizer cases (%) , means	AstraZeneca cases (%) , means	Sinopharm cases (%) , means	All specimens, means
IgG pre-vaccination	3.11	3.15	3.09	3.12
IgA pre-vaccination	2.81	2.31	2.63	2.40
IgG after 1 <sup>st</sup> dose (25 days)	10.99	8.67	5.41	7.78
IgA after 1 <sup>st</sup> dose (25 days)	12.01	10.44	7.45	9.08
IgG after 2 <sup>nd</sup> dose (50 days)	22.05	18.21	9.93	13.93
IgA after 2 <sup>nd</sup> dose (50 days)	23.11	20.01	11.12	17.03



**Figure 2.** Adverse effects of Pfizer, AstraZeneca, and Sinopharm recipients. A) Adverse marks were found after the first dose in the studied group. The percentage of cases is represented by the values in each column. B) Adverse marks were found after the second dose in the studied group. The percentage of cases is represented by the values in each column.

(25%). However, chills, sleepiness, and the flu-like syndrome were the most common side effects among the recipients who received the first dose of the BBIBP-CorV vaccine, as compared to the Pfizer and AstraZeneca vaccine.

**IgG levels upon Pfizer, AstraZeneca, and Sinopharm vaccination**

The level of IgG significantly differed between the three studied groups (Table 2). People who had the first and second shots of the Pfizer vaccine had a higher level of IgG than those who had the doses of the AstraZeneca vaccine. before the vaccination program, the IgG level in previously infected people was slightly increased to more than 3 grade by infection of SARS-CoV-2. After receiving the first and second doses of these three vaccines, the IgG level was increased 3 times higher. The first dose of the Pfizer vaccine could increase more than 7 grades of the IgG level, as compared to AstraZeneca, which increased more than 5 grades. The second dose of Pfizer could boost 12 grades of IgG level compared to the AstraZeneca, which increased the 10 grades (Figure 3A). However, the IgG level in BBIBP-CorV vaccine recipients was significantly lower than 5 grade (for the first dose) and 9 grade (for second dose). These grades were markedly lower than those who received the Pfizer and AstraZeneca vaccine. Scatter plots showed that a positive correlation was found between the first and second doses of Pfizer, AstraZeneca and Sinopharm vaccines. The positive correlation between the first and second doses of the Pfizer vaccine was  $r=0.041$ , with  $P=0.001$  (Figure 3B) and AstraZeneca was  $r=0.024$ , with  $P=0.001$  (Figure 3C); whereas, the association between first and second doses of Sinopharm was  $r=0.07$ , with  $P=0.02$  (Figure 3D).

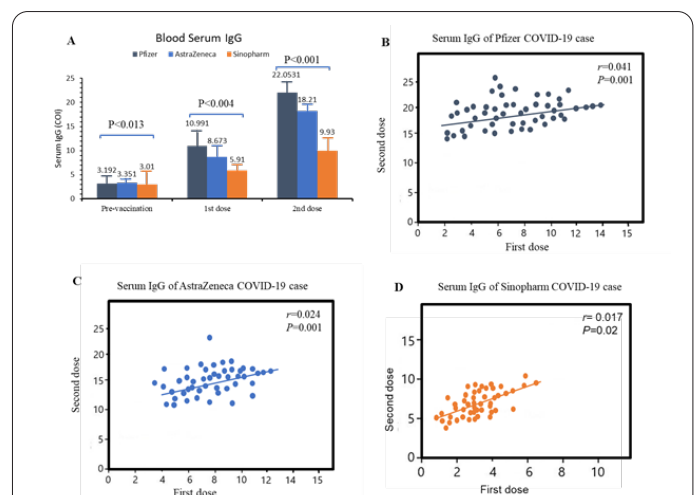
However, the IgG levels in Pfizer recipients were de-

tected to rise about 18 times in males and almost 7 times in females after the first immunization dose. When compared to the first shot, the IgG levels increased 6.42 times in males and 3.04 times in females after the second shot of vaccination. Although the IgG response in males appeared to be stronger at 25 days than in females, after the second shot of vaccination, the IgG serum in both Pfizer and AstraZeneca vaccines appeared to homogenize, indicating that the produced immune response has a plateau that is achieved by all infected participants. When comparing pre-vaccination and first dose (after 25 days) to recorded levels after 30 days, the increase in IgG level after vaccination is statistically distinct. Regarding the infected group, it was found that a 3.62-fold rise in males and a 2.01-fold increase in females following the first shot of vaccination (Figure 3A). Males experienced a 4.52-fold increase after the second dose, while females experienced a 3.13-fold increase. It appears that the total vaccination of the Pfizer vaccine boosted greater IgG levels in both males and females when compared to the AstraZeneca vaccine. When comparing pre-vaccination with levels after 21 days and IgG levels after 21 days vs 45 days registered levels in previously infected participants, the increase in IgG level is significantly different (Figure 3A).

**IgA levels upon Pfizer, AstraZeneca Sinopharm vaccination**

Vaccines of Pfizer and AstraZeneca produced higher levels of IgA in the blood of vaccination recipients, just as they did with IgG. These values were much greater in Pfizer patients than AstraZeneca and Sinopharm patients (Table 2). After the first and second doses of vaccination, the levels of IgA in both Pfizer and AstraZeneca recipients appeared to be significantly higher when compared to the level of IgA in the patients who received the BBIBP-CorV (Figure 4). When IgA levels were compared to IgG levels using statistics in all infected patients, the results were almost resembled (Table 2).

When the IgA values obtained by the Pfizer and As-



**Figure 3.** Analysis of IgG serum generated by Pfizer, AstraZeneca, and Sinopharm vaccines in previously infected participants. (A) The IgG level (COI) in Pfizer, AstraZeneca, and Sinopharm recipients, after the first and second doses. (B) Correlation between the first and second doses of the IgG levels of Pfizer recipients. (C) Correlation between the first and second dose of IgG levels of AstraZeneca recipients. (D) Correlation between the first and second dose of IgG levels of Sinopharm recipients.

traZeneca vaccinations were compared to the infected patients' serum IgG levels, the initial vaccine dosage resulted in a higher amount of IgA in the infected group. The IgA levels in the infected group increased more than serum IgG levels after the second dosage of both vaccines. However, the IgA response to the Sinopharm vaccine slowly increased following both 1<sup>st</sup> and 2<sup>nd</sup> doses, as compared to the spike antigen-specific IgG.

While men and women appear to have similar improvements in serum IgA, the mean value reached by men subjects after the second dose of the Pfizer and AstraZeneca immunization is larger than that of women. The first shot increases serum IgA levels in both men and women, with males (5.6 times) and women (4.32 times) correspondingly. The second dose produces the highest recorded levels in both men and women at similar amounts (Figure 4).

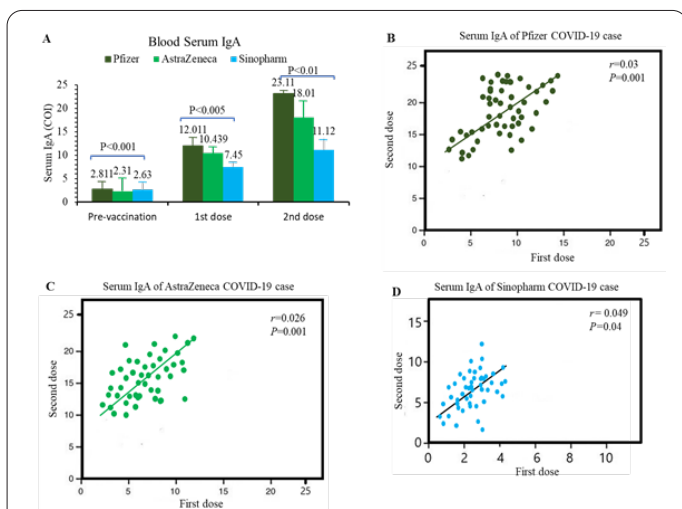
The results for the three vaccinations were analyzed as previously described, and the dispersion of individual blood IgG levels for each vaccine was displayed in Figure 5A at pre-vaccination, 25 days, and 30 days. Similarly, Figure 5B depicted the dispersion of individual serum IgA distributions for each participant at pre-vaccination, after 25 days, and after 30 days.

The rise in levels of serum IgG and IgA after the prime and boost of Pfizer, AstraZeneca and BBIBP-CorV immunization were comparable across the board, regardless of prior exposure to the infectious agent (Figure 6).

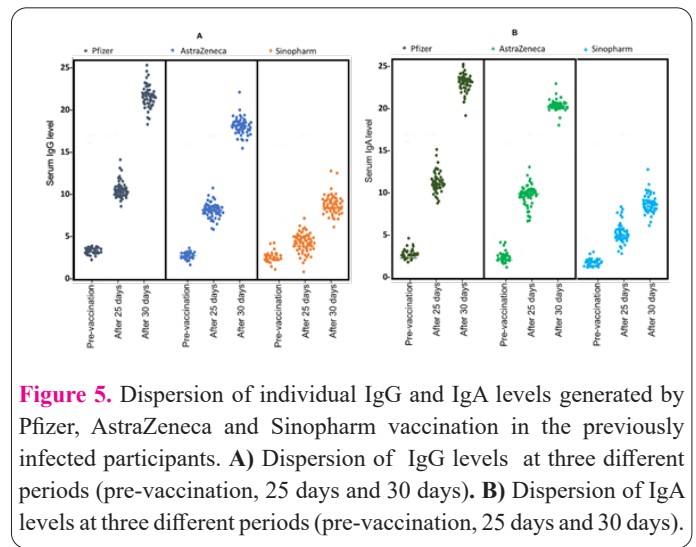
Seroconversion was obtained in 99 percent of participants for serum IgG and 83 percent for serum IgA after the first dosage, and in 100 percent of the entire group after the boost, with extremely similar antibody levels.

**Antigen-specific IgG and IgA response to the novel COVID-19 vaccines**

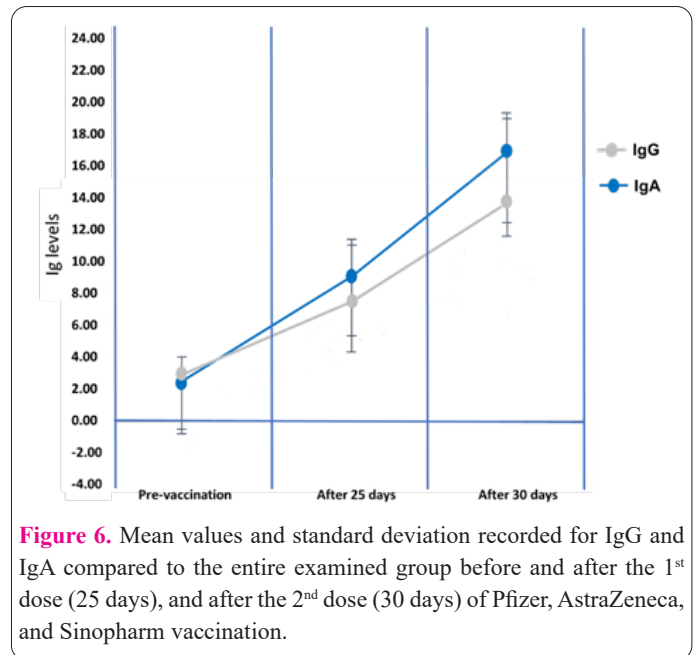
Blood levels of SARS-CoV-2 spike antigen-specific IgG and IgA were assessed using the ELISA technique in 150 previously infected cases that were vaccinated with Pfizer, AstraZeneca and Sinopharm vaccine. As shown in



**Figure 4.** Analysis of IgA serum generated by Pfizer, AstraZeneca, and Sinopharm vaccines in previously infected participants. (A) The IgA level (COI) in Pfizer, AstraZeneca, and Sinopharm recipients, after the first and second doses. (B) Correlation between the first and second doses of the IgA levels of Pfizer recipients. (C) Correlation between the first and second dose of the IgA levels of AstraZeneca recipients. (D) Correlation between the first and second dose of the IgA levels of Sinopharm recipients.



**Figure 5.** Dispersion of individual IgG and IgA levels generated by Pfizer, AstraZeneca and Sinopharm vaccination in the previously infected participants. **A)** Dispersion of IgG levels at three different periods (pre-vaccination, 25 days and 30 days). **B)** Dispersion of IgA levels at three different periods (pre-vaccination, 25 days and 30 days).



**Figure 6.** Mean values and standard deviation recorded for IgG and IgA compared to the entire examined group before and after the 1<sup>st</sup> dose (25 days), and after the 2<sup>nd</sup> dose (30 days) of Pfizer, AstraZeneca, and Sinopharm vaccination.

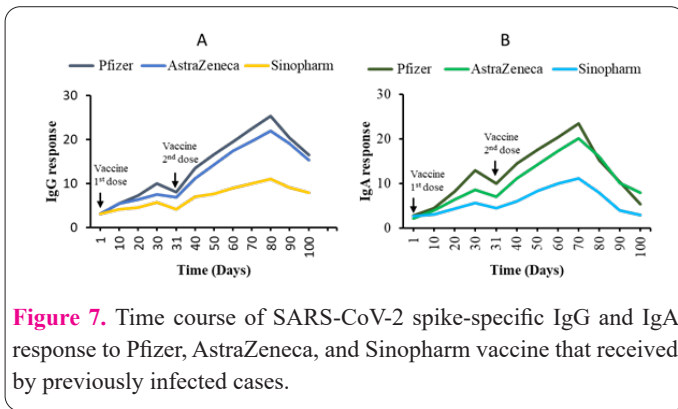
Figure 7A, the serum level of SARS-CoV-2 spike-specific IgG caused by Pfizer and AstraZeneca vaccine was significantly increased and reached a pick about 25-30 days following the 1<sup>st</sup> dose, as compared to the level of SARS-CoV-2 spike-specific IgG caused by BBIBP-CorV vaccine. This first immune response is called the primary immune response.

The serum level of SARS-CoV-2 spike-specific IgG grew further, peaking about 10 days later, and continuing to increase (80% of peak values) during the other 25-50 days follow-up period.

Similar to the serum level of SARS-CoV-2 spike-specific IgG caused by Pfizer and AstraZeneca vaccine, they also produced spike antigen-specific IgA with similar kinetics of induction and time to maximal levels after the 1<sup>st</sup> and 2<sup>nd</sup> vaccine dose (Figure 7B). However, the levels of spike antigen-specific IgA reduced significantly ( $p < 0.01$ ) faster than the serum IgG levels. Spike-specific IgA decreased to get lower than 40% peak levels between the 1<sup>st</sup> and 2<sup>nd</sup> doses, and 40% of peak levels within the 45-day follow-up period after the 2<sup>nd</sup> shot.

**Genomic analysis of COVID-19 vaccines**

More than 100 nucleotide sequences of SARS-CoV-2 strains were downloaded from the National Center of Bio-



**Figure 7.** Time course of SARS-CoV-2 spike-specific IgG and IgA response to Pfizer, AstraZeneca, and Sinopharm vaccine that received by previously infected cases.

technology Information (NCBI) database to know whether the Pfizer, AstraZeneca and Sinopharm vaccine is effective or not. There are three strains named 19nCoV-CDC-Tan-Strain03 (CQ01), 19nCoV-CDC-Tan-Strain04 (QD01), and 19nCoV-CDC-Tan-HB02 (HB02) have been distributed in the world (Figure 8). All of which are distributed on the phylogenetic tree created from all available sequences, indicating that they cover the main SARS-CoV-2 populations. Because the SARS-CoV-2 virus is transmitted from person to a person, all the strains from different continents have been closely evolutionarily related and homologous to each other. They have been certified by WHO for the construction of vaccine. Genetically, the whole genome of the HB01 strain was completely identical to other SARS-CoV-2 strains from around the world. As a result, the HB02 strain was selected to construct the inactivated SARS-CoV-2 vaccine (BBIBP-CorV). Sequence alignment revealed the gene codes for spike protein in the HB02 strain are homologous to other viral strains and have 100% homology. For this reason, the BBIBP-CorV vaccine has been able to work on the residents of the Kurdistan region in Iraq.

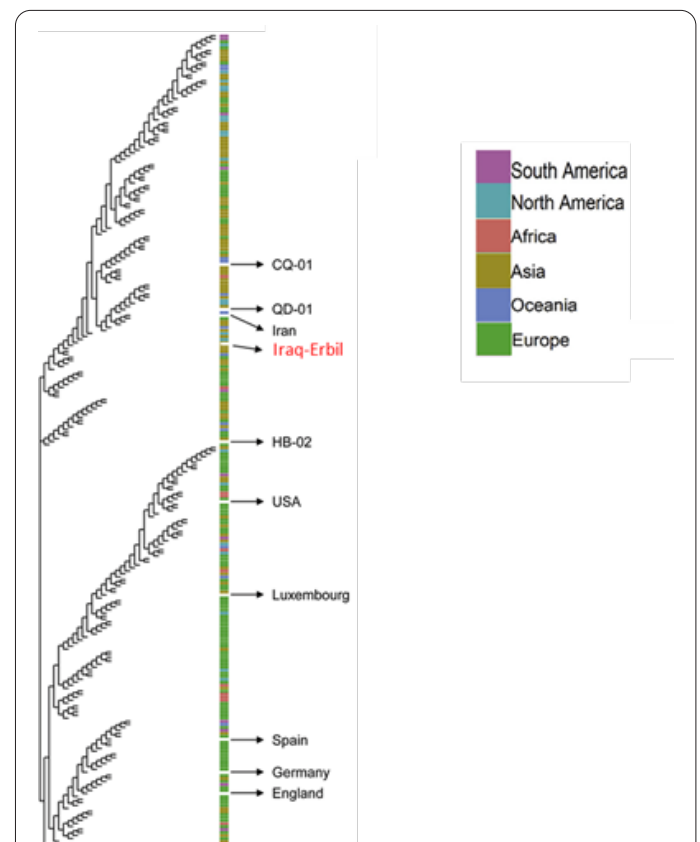
Instead of using the whole virus, another approach to trigger immunity involves using just fragments of the SARS-CoV-2 virus, such as the spike proteins. Langer, Anderson, and colleagues produced lipid nanoparticles, which are fatty polymers that are also very effective in delivering nucleic acids, in subsequent years. These carriers serve to transport messenger (m)RNA through cell membranes and protect it from being broken down in the body. Lipid nanoparticles containing polyethylene glycol (PEG) are used in both the Moderna and Pfizer RNA vaccines. These subunit vaccines have the advantage of being relatively easy and cheap to produce. They are incapable of causing disease because these fragments are not able to infect host cells and also are less likely to be recognized by immune cells and are aimed at attacking infected cells; which means they may trigger a weaker immune response. Because of this, mRNA vaccines often include chemical agents called adjuvants, which are designed to stimulate a stronger immune response and a booster shot may also be required.

## Discussion

Several approved vaccines are already used in the vaccination programs around the world. In the present study, the effectiveness and efficacy of mRNA-based vaccine (Pfizer-BioNTech) made by Pfizer, and viral vector vaccine (AstraZeneca) made by (Oxford) were analyzed and

determined by assessing anti-SARS-CoV-2 spike-specific IgG and IgA antibodies from people who had previously been infected with COVID-19. Another mRNA-based vaccine designed by Moderna company has the capability to boost humoral and cellular immunity. ChAdOx1 (scientific name AZD1222 or AstraZeneca) is a different type of vaccination. This form of the mRNA-based vaccine is unique in that it is based on a replication-deficient simian adenovirus vector that contains the S glycoprotein gene (15, 16). As a result, the COVID-19 vaccines, which are widely used around the world, appear to elicit the desired particular immune response. There are also questions about how long this immunity would provide protection and whether the new variations that emerge will be neutralized by the antibodies generated against current vaccine platforms (17). Data suggest that these vaccines cause a considerable rise in antibodies to the spike protein of SARS-CoV-2 and its variants currently circulating in the world, at least for the time being. As a result, there is good news in terms of a specialized immune response that can combat various viral variations, including potentially new ones.

However, vaccines purified from virally infected cells are inactivated virus vaccinations, which are a traditional way of making vaccines. They're usually generated by exposing virulent viruses to chemical or physical agents, such as formalin or -propiolactone, to knock down infectivity while keeping immunogenicity (18). The Beijing Institute of Biological Products (Beijing, China) produced the BBIBP-CorV (Sinopharm), an inactivated SARS-CoV-2



**Figure 8.** SARS-CoV-2 Maximum Likelihood Phylogenetic Tree. The SARS-CoV-2 isolates used in this study are indicated with black arrows and labeled. The viral strain was isolated from an infected patient in Iraq-Erbil (red label). Viral strains were isolated from infected patients who traveled from the indicated continent/area. MEGA11 software was used to construct.

vaccine candidate with aluminum as an adjuvant (18) (19). In rats, mice, guinea pigs, rabbits, cynomolgus monkeys, and rhesus macaques, this candidate vaccination elicited high levels of neutralizing antibodies, protecting them against SARS-CoV-2 infection. The neutralizing antibody levels in mice in the low-dose (two g/dose) and middle-dose (four g/dose) groups showed substantial variance at seven, fourteen, and twenty-one days, however no significant variation was seen in the high-dose (eight g/dose) group (19).

A recent study showed that seroconversion was observed in all participants receiving the Sinopharm vaccine of stage I and II trials. It was also detected that the majority of participants after the second injection began to produce antibody responses, which remained high fourteen days later. Furthermore, the neutralizing antibody response was monitored for two weeks days following the injections, indicating that the Sinopharm vaccine could effectively induce antibody production. The most common adverse reaction was injection site pain, followed by mild and self-limiting fever. Furthermore, the BBIBP-CorV vaccine, administered in two doses, was safe and well tolerated, and humoral responses against SARS-CoV-2 were induced in 100% of vaccinees by day 45. During stage II, the Sinopharm vaccine was administered (19).

Because ELISA testing is used in the majority of serological assays, it was used in the present investigation. The ELISA test we used (EUROIMMUN Anti-SARS-CoV-2 ELISA Assay) has been evaluated, validated, and is on the FDA's list of immunoassays to use in pandemics currently underway (20). This methodology was found to have high sensitivity for detecting IgA and excellent sensitivity for detecting IgG as early as four days after RT-PCR diagnosis of COVID-19, with no crosser activity to human coronavirus infection(21, 22). Seroconversion in the present investigation was achieved in 98.5 percent of recipients after the first shot of IgG and 81 percent after the second shot of IgA, and in 100 percent of the group after the boost, with highly similar antibody levels; these results were similar to those of a recent report on a small, vaccinated group of oncological patients (23, 24).

There was no link between gender and post-vaccination level, just as there was no link between the severity of ill effects and earlier contact with the viral agent. Even though the presence of unfavorable effects appeared to be slightly higher in diseased subjects compared to naive subjects(24). We cannot rule out the possibility that a bigger sample size might have revealed statistical differences related to age and gender. Similar findings revealed that post-vaccine symptoms were more significant for previously infected participants after the first shot in a group of the same vaccine recipients, but overall symptomology was similar between groups following the second shot (25).

The levels of IgG and IgA in participants who still had positive levels after infection were moderately higher after the first and second shots than in uninfected subjects. Specific IgG antibody levels elicited by a single vaccine dosage in past SARS-CoV-2 infected people were identical to those detected after two vaccine shots in people without prior infection, according to findings published in April 2021(26).

A study in health care staff found that following the first dosage of the Pfizer-BioNTech vaccine, the prior infected people' total antibodies increased more than 140-fold in

contrast to their pre-vaccine levels in a nested case-control analysis within the COVID-19 (fifty-one participants)(26).

Even though the IgG and IgM antibodies are the most commonly evaluated in COVID-19 disease, circulating IgA levels may provide useful information into the humoral immunity course generated in both infected and vaccinated patients. IgA is the most common antibody class generated in humans, and it plays a vital role in antimicrobial defense by neutralizing pathogens that attack the mucosal barrier (30). IgA is divided into several subclasses (IgA1/IgA2) and isoforms (monomeric, dimeric, and secretory) (27). While monomeric IgA1 (85%) is the most common form of IgA in circulation and is considered an anti-inflammatory isotype, dimeric/secretory IgA has both pro and anti-inflammatory properties (28).

Although IgA defines the humoral immunity profile at the mucosal level, it is underutilized in the COVID-19 setting to fully outline the immune response and is almost completely neglected in post-vaccination investigations. Because the nature and function of IgA in SARS-CoV-2 infection is unknown, testing serum IgA-specific antibodies in both infected and hence vaccinated people is of special interest. Antibody responses to SARS-CoV-2 spike antigens have also been documented in serum and saliva (29). In order to define largely the asymptomatic and moderate cases that often reflect COVID-19 infections, the measurement of circulating IgA antibodies is just as important as IgG testing in COVID-19 (30).

To the best of our understanding, no data on IgA circulating levels in vaccinated people exists, and just a few in distinct COVID-19 forms (31). SARS-CoV-2 blood IgA occurrence requires an average seroconversion interval of 25 days after symptom onset (32), and it is related to early action in SARS-CoV-2 infection, being even more effective than IgG in neutralizing SARS-CoV-2. In terms of IgA persistence in the blood, a recent study found that the circulating anti-spike IgA could last up to 8 months after SARSCoV2 infection. The researchers also noticed that the levels of IgG and circulating IgA remained positive in the oldest infected person (33).

The monomeric/dimeric form of IgA has recently been linked to the potency of serum IgA vs IgG in SARSCov2 infection. Specifically, serum monomeric IgA is approximately two times less effective than IgG, whereas mucosal dimeric IgA is substantially more effective than monomer IgA in neutralizing SARSCoV2 (34, 35).

Several possibilities arose from the analysis of serum IgG levels in previously infected participants who have inoculated with the Pfizer (BNT162b2) vaccine vs people who were inoculated with the AstraZeneca (AZD1222) vaccine. In comparison to the IgG levels achieved by individuals inoculated with AstraZeneca vaccine (IgG mean,8.67), Pfizer immunization causes higher levels of IgG following the first dose of vaccination in not infected patients (IgG mean,10.99). prior to vaccination, the total mean IgG level in people who were infected with COVID-19 was increased to 3.1. Because of the increase in IgG levels in Pfizer-vaccinated participants 33 percent larger than the IgG levels obtained by Oxford-AstraZeneca-vaccinated participants, the vaccination of individuals with COVID-19 prior to immunization must be suggested. prior to vaccination, the total mean IgG level in people who were infected with COVID-19 was increased to 3.1, but the total IgA was increased to 2.4. The second shoot

(boost) of the Oxford-AstraZeneca vaccine elicits slightly lower antibody responses (IgG mean ,18.21) in previously infected participants than the second dose of the Pfizer vaccine (IgG mean, 22.05). When compared to AstraZeneca-vaccinated participants for the first shot, Pfizer-vaccinated participants had IgG levels that are 12.05 percent higher for the first shot (36).

The second shot of immunization boosts IgG levels in Pfizer-vaccinated participants by up to 30.18% (relative to the first dose of the Pfizer vaccine) and by 20.18% in AstraZeneca-vaccinated participants. The need for a second vaccine dose in people infected with COVID-19 can be disputed based on this finding. The humoral immunity with the ability to protect against COVID-19 disease achieved in these participants after the first vaccine injection is outstanding, but a second shot has the potential to fuel it. Given these findings and the global shortage of vaccine doses, it's possible that the time between the first and second doses of the vaccine for those who have already been infected with SARS-CoV-2 could be extended (37).

Similarly, to the discussion of IgG levels, the outcomes for IgA levels may have some unique values that should be highlighted. The IgA levels may be linked to transmission capacity because it is primarily involved in local protection. Prior to the vaccination process, the total mean of IgA levels in participants who had previously been infected with COVID-19 was 2.4, but after the first dose of Pfizer vaccination, the participants had greater levels of IgA (IgA mean, 2.81) than AstraZeneca-vaccinated people (IgA mean, 2.30) (38).

However, the surge in IgA levels in Pfizer-vaccinated participants after the second shot was higher than after the first shot (with 30.14 percent). The second dose of immunization boosted IgA levels in AstraZeneca-vaccinated participants by nearly half (15.19 percent) when compared to IgA levels after the first dose. The surge in IgA levels in Pfizer-vaccinated participants after the second shot was higher than the IgG levels in those who were vaccinated with AstraZeneca after the second shot (with 40.14 percent). In summary, the second shot of both Pfizer and AstraZeneca immunization generated a robust IgA response that may provide supplemental protection against SARS-COV-2 transmission, reduction of death rate and hospitalization (39).

The importance of serology testing is emphasized before vaccination protocol in order to promptly assess the participants' humoral and cellular immune status and alter the immunization procedure accordingly. A new study shows that Pfizer and AstraZeneca vaccines were highly effective and strong at boosting humoral and cellular immunity. The results of this study agree with the findings of the present study that have been revealed. Two current studies show that the Pfizer-BioNTech vaccine and CHAdOx1 (Oxford-AstraZeneca) vaccine are highly efficacious and safe at protecting people from the adverse risks of the COVID-19 pandemic, hospitalization, and death. The results show that both vaccines could lead to a strong immune response against SARS-CoV-2 (40-42). Another study reveals that the infection with COVID-19 reduced to 65% after receiving the prime and boost of mRNA-based vaccine made by Pfizer and AstraZeneca vaccine, which utilizes adenovirus to deliver instructions for tissues to make a SARS-CoV-2 protein According to another study, the participants' antibody response to the mRNA-based

vaccine appears to be higher and stronger than participants receiving two doses of the Oxford–AstraZeneca vaccine (43). According to a new study, the Pfizer-BioNTech vaccination in COVID-19-infected recipients can result in much greater immunoglobulin G (IgG) and immunoglobulin A (IgA) levels than the Oxford-AstraZeneca vaccine (44).

## Conclusion

Anti-SARS-CoV-2 spike-specific antibodies in patients who had previously been infected with COVID-19 were measured before and after vaccination in this work. When compared to the adverse effects generated by the Sinopharm vaccine, the adverse effects of Pfizer and AstraZeneca were Fatigue, and fever, followed by headache and injection site pain. Furthermore, the BBIBP-CorV vaccine, administered in two doses, was safe and produced a low level of humoral responses against SARS-CoV-2 in all vaccinees. However, all of the test subjects had high levels of anti-spike-specific IgG and IgA after receiving the first and second shots of the Pfizer, and AstraZeneca vaccines. The vaccine elicited statistically equal levels of antibodies regardless of previous illness. Seroconversion was achieved in all vaccinees after the vaccination procedure was completed, with highly identical antibody levels for both tested antibodies.

## Author Contributions

S.O.M. completed every study-related task, including data collection, analysis, and manuscript drafting. He also wrote the main manuscript, and revision.

## Acknowledgments

We thank the staff and management team of Nawroz Hospital Center.

## Conflicts of Interest

The authors declare no competing interests.

## Funding

This study received no external funding.

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