Original Article

Assessment of Some Immunological Parameters Postvaccination with Different Types of COVID-19 Vaccines

Haneen Saad Khasbak, Hayder Shkhair Al-Janabi, Mohanad Jawad Kadhim
Department of Medical Biotechnology, College of Biotechnology, Al-Qasim Green University, Babylon, Iraq

Abstract

Background: Coronavirus disease 2019 (COVID-19) is a highly contagious viral infection that can spread rapidly worldwide. Several vaccines have been developed to combat COVID-19. **Objectives:** This study aimed to assess some immunological parameters, including $CD8^+$ and IgG levels in sera of different vaccinated groups with different types of COVID-19 vaccines. **Materials and Methods:** The current study included 75 samples from vaccinated persons with AstraZeneca, Sinopharm, and Pfizer vaccines and 25 unvaccinated (naturally infected) persons. $CD8^+$ and IgG levels were measured using ELISA technique. **Results:** The results showed that the $CD8^+$ level increased significantly ($P < 0.05$) in the Pfizer vaccinated group than in Sinopharm and AstraZeneca groups, and there were no significant differences in the $CD8^+$ level in the Pfizer-vaccinated group and unvaccinated group. The results also showed significant differences between $CD8^+$ levels in males (22.78 ± 3.36) and females (9.86 ± 1.16) in Sinopharm vaccine, whereas there were no significant differences in $CD8^+$ levels between males and females in other vaccine groups. COVID-19 IgG antibody levels were elevated significantly in unvaccinated people compared to those who received the Pfizer vaccine. In contrast, there were no significant differences in concentration of IgG antibodies between Sinopharm, AstraZeneca vaccines, and unvaccinated groups. Notably, the Pfizer vaccine exhibited significantly lower IgG levels in all age groups compared to the other vaccines. **Conclusion:** The Pfizer vaccine induced a cellular immune response represented by $CD8^+$ levels than other COVID-19 vaccines and unvaccinated (naturally infected) people, while natural immunization had higher IgG by inducing a humoral immune response than COVID-19 vaccines.

Keywords: AstraZeneca, $CD8^+$, COVID-19, IgG, Pfizer, Sinopharm

Introduction

COVID-19 is highly contagious and can spread rapidly throughout the world.[1] It was found to be quite similar to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[2] It has been categorized as a member of the Orthocoronavirinae subfamily of the Betacoronavirus genus and placed in the subgenus Sarbecovirus.[3]

Coronaviruses are enclosed, large, single-stranded RNA viruses.[4] It contains four main structural elements: envelope (E), membrane (M), spike (S), and nucleocapsid (N) proteins.[5] The coronavirus is so named because of the "corona" spikes that the S-glycoprotein protrudes from the viral capsid.[6] The spike glycoprotein of SARS-CoV-2 binds to the host cell receptor angiotensin-converting enzyme 2 (ACE2), which is necessary for cell entry.[5]

Innate and adaptive immune responses are two types of immunological responses.[7] Activation of the host defense system is caused by the stimulation of TLRs through contacts with ligands, which start an intracellular downstream signaling cascade representing the innate immune system.[8] TLR7/8 detects SARS-ssRNA CoV-2, and following replication, the viral dsRNA is recognized by TLR3, which triggers TRIF-mediated inflammatory signaling.[8] This enhances the expression of target genes, such as types I and III IFNs and several other critical pro-inflammatory cytokines.[8] Adaptive immune responses

Access this article online

Quick Response Code:

Website: https://journals.lww.com/mjby

DOI: 10.4103/MJBL.MJBL_1178_23

Address for correspondence: Prof. Dr. Mohanad Jawad Kadhim, Department of Medical Biotechnology, College of Biotechnology, Al-Qasim Green University, Babylon 5103, Iraq.
Email: dr.mohanad@biotech.uoqasim.edu.iq

Submission: 11-Aug-2023 **Accepted:** 21-Dec-2023 **Published:** 28-Jun-2025

How to cite this article: Khasbak HS, Al-Janabi HS, Kadhim MJ. Assessment of some immunological parameters postvaccination with different types of COVID-19 vaccines. Med J Babylon 2025;22:418-25.

(both T and B cells) against SARS-CoV-2 start to be visible around a week after the onset of symptoms. T-cells have two main functions: $CD8^+$ T-cells actively target and kill virus-infected cells, whereas $CD4^+$ T-cells prime both B cells and $CD8^+$ T-cells as well as produce cytokines that aid in the recruitment of immune cells.[9] T helper cells enable B cells to develop into plasma cells, which in turn manufacture antibodies (Abs) targeted to a viral antigen (Ag) called Neutralizing antibodies. In the case of SARS-CoV, the antibody profile of this virus produces IgM and IgG, and at a later phase, seroconversion, which is mediated by the helper T-cells, has been found. The helper T-cells also play a role in isotype switching.[9] It was observed that cellular immunity had a significant role in defending against SARS-CoV-2 due to the high number of $CD8^+$ infiltrating cells (80%) recruited to the infection site.[10] Recent findings indicate that specific IgG-neutralizing antibodies targeting the spike protein's receptor-binding domain (RBD) can effectively prevent the fusion between the virus and ACE2 receptors, blocking viral entry into lung cells and further transmission.[11] In another study, they examined the features of CD4+ and $CD8^+$ T-cell immune responses among confirmed COVID-19 cases. They observed that 100% of CD4+ T-cells were activated in response to the spike protein and that the anti-SARS-CoV-2 IgG and IgA titers were associated with the spike protein response's intensity.[12]

Several technologies are used to create COVID-19 vaccines, including mRNA (the Moderna and Pfizer vaccines), adenoviral vector (the Johnson & Johnson and AstraZeneca vaccines), inactivated whole-virus vaccines (the Sinopharm vaccine), and a subunit vaccine (Novavax, USA). Each one of them depends on the SARS-CoV-2 native viral spike protein (S) to stimulate powerful neutralizing antibodies.[13] Following immunization, high-affinity SARS-CoV-2 antibodies as well as memory T and B cells specific for the S protein, form and circulate, all of which work to prevent further SARS-CoV-2 infection.[14]

This study aimed to assess $CD8^+$ and IgG levels in different vaccinated groups with COVID-19 vaccines.

Materials and Methods

Study of design and participants

One hundred blood samples were collected, including 75 persons vaccinated with AstraZeneca (25), Sinopharm (25), and Pfizer (25) (after the second dose of all vaccines) and unvaccinated (25) (natural immunization or infected) persons. The samples were not infected except for unvaccinated persons who had previous infections. Samples were collected between August 1, 2022, and December 1, 2022, from the medical and work staff at Marjan Teaching Hospital, Al-Hilla Teaching Hospital, Imam Al-Sadiq Hospital, and from residential areas in the Babylon Province. All individuals included in this study were between the ages of 20 and 55 years. The personal information collected from each person included name, age, gender, place of residence, academic achievement, the type of vaccine received, whether they had previously been infected, the dates of the first and second vaccine doses, the type of vaccine symptoms experienced, the duration of vaccination, smoking status, pregnancy status in women, any chronic diseases, the duration of COVID-19 infection period, and whether the infection occurred before or after vaccination. Three milliliters of blood were collected from all samples, placed in a gel tube for serum separation, left to clot at room temperature, and centrifuged at 4000 rpm for 2 min. The serum was transferred into an Eppendorf tube and stored at –20°C.[15]

Measurement of a serological assay

Sandwich ELISA kit was used to measure the $CD8^+$ and SARS-CoV-2 IgG levels in sera from different vaccinated sample groups, according to Elabscience (Houston, TX).

Statistical analysis

Statistical analysis was carried out using the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL) version 26, along with Microsoft Excel Worksheet. The findings and illustrations of the present study were subjected to thorough examination. Significance with regards to P value was ascertained for values below 0.05 ($P < 0.05$).

Ethical approval

The research was carried out in adherence to the ethical guidelines rooted in the Declaration of Helsinki. The procedural details of the study, as well as the information provided to participants and the consent form, were thoroughly reviewed and approved by a local ethics committee under reference number 1742 on November 24, 2022, to obtain the necessary authorization.

Results

$CD8^+$ level among COVID-19 vaccines and unvaccinated (naturally infected) persons

The serum levels of $CD8^+$ were detected among individuals who received different COVID-19 vaccines and those who were unvaccinated but were infected with the virus. Results showed that individuals who received the Pfizer vaccine had a higher $CD8^+$ concentration (34.579 ± 7.89 ng/mL) compared to those who received the AstraZeneca vaccine and Sinopharm vaccines (16.389 ± 2.26 and 17.618 ± 2.41 ng/mL, respectively) with significant differences ($P < 0.05$). Unvaccinated individuals who were infected with the virus had a $CD8^+$ concentration (23.304 ± 3.126 ng/mL), which was lower than that of the Pfizer vaccine but higher than that of the Sinopharm and AstraZeneca vaccines (17.618 ± 2.41 and 16.389 ± 2.26 ng/mL, respectively) without significant differences ($P < 0.05$) as illustrated in Figure 1.

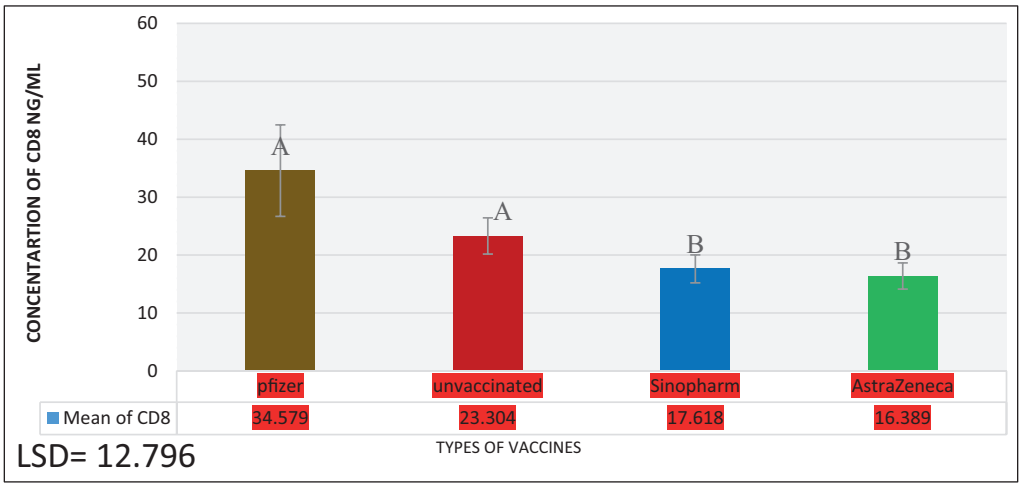

Figure 1: The concentration of CD8 (ng/mL) among COVID-19 vaccines and unvaccinated (naturally infected) persons

Table 1: CD8⁺ levels (ng/mL) among males and females who received different types of COVID-19 vaccines and unvaccinated (naturally infected) persons

Type of vaccine	Group		
	Males	Females	*P* value (*P* < 0.05)
AstraZeneca	16.32 ± 2.46[a]	16.56 ± 5.35[a]	0.234
Sinopharm	22.78 ± 3.36[a]	9.86 ± 1.16[b]	0.023
Pfizer	35.78 ± 10.34[a]	33.47 ± 12.21[a]	0.792
Natural immunization	27.15 ± 4.61[a]	20.27 ± 4.2[a]	0.689

Similar letters indicate non-significant differences, while different letters indicate significant differences

CD8⁺ level between different COVID-19 vaccines and unvaccinated persons according to gender

The study examined the differences in CD8⁺ levels between males and females who received various COVID-19 vaccines, as well as those who were unvaccinated but had been infected with the virus. The findings showed that females who received the AstraZeneca vaccine had a slightly higher concentration of CD8⁺ than males (16.56 ± 5.35 and 16.32 ± 2.46 ng/mL, respectively), but these differences were not significant ($P > 0.05$). In contrast, males who received the Sinopharm vaccine had significantly higher ($P < 0.05$) levels of CD8⁺ compared to females (22.78 ± 3.36 and 9.86 ± 1.16 ng/mL, respectively). Similarly, in the case of the Pfizer vaccine, males had higher CD8⁺ levels than females (35.78 ± 10.34 and 33.47 ± 12.21 ng/mL, respectively), but this difference was not significant compared to unvaccinated individuals who had been infected with the virus that males significantly higher than females (27.15 ± 4.61 and 20.27 ± 4.2 ng/mL) ($P < 0.05$). Also, the results showed that both males and females groups who were vaccinated with the Pfizer vaccine had a significantly higher level of CD8⁺, while males and females groups in the AstraZeneca vaccine had the lower concentration of 16.32 ± 2.46 and 16.56 ± 5.35, respectively, with $P < 0.05$. The results are presented in Table 1.

The level of CD8⁺ (ng/mL) according to the age groups

Table 2 shows that individuals aged 20–29 who received the Pfizer vaccine had the highest CD8⁺ levels (51.89 ± 14.24 ng/mL) with significant differences ($P < 0.05$), while unvaccinated individuals who had been infected with the virus had the lowest CD8⁺ levels (19.19 ± 4.11 ng/mL). AstraZeneca had slightly higher CD8⁺ levels (13.87 ± 4.05ng/mL) than Sinopharm (13.07 ± 2.02 ng/mL) with no significant differences ($P > 0.05$).

For individuals aged 30–39 years, unvaccinated individuals who had been infected with the virus had higher CD8⁺ levels (29.78 ± 7.51 ng/mL) compared to those who received the Pfizer vaccine, which was lower in CD8⁺ level (16.09 ± 2.41 ng/mL) with significant differences ($P < 0.05$). The differences between AstraZeneca (19.27 ± 5.97 ng/mL) and Sinopharm (19.22 ± 4.75 ng/mL) were not significant.

The age group of 40–49 years, who received the Pfizer vaccine, had higher CD8⁺ levels (32.39 ± 13.19 ng/mL), while those who received the AstraZeneca vaccine had lower CD8⁺ levels (18.82 ± 7.81ng/mL) with significant differences ($P < 0.05$). In contrast, the Sinopharm vaccine had higher CD8⁺ levels (29.38 ± 11.75 ng/mL) than unvaccinated individuals who had been infected with the virus (22.18 ± 8 ng/mL).

Finally, for the age group 50–59 years, unvaccinated individuals who had been infected with the virus had higher CD8⁺ levels (32.78 ± 9.5 ng/mL) compared to those who received the Pfizer vaccine that had the less CD8 level (11.82 ± 4.86 ng/mL) with significant differences ($P < 0.05$). The sinopharm vaccine was higher than the AstraZeneca vaccine in the CD8⁺ level (17.48 ± 1.72 and 16.55 ± 3.29 ng/mL) with no significant differences ($P > 0.05$).

IgG Concentration (mg/dL) among COVID-19 vaccines and unvaccinated persons

This study compared IgG concentrations between individuals who received different COVID-19 vaccines

Table 2: CD8⁺ Levels (ng/mL) in various types of COVID-19 vaccines and unvaccinated individuals (naturally infected), stratified by age groups

Age groups (years)	Type of vaccine				
	NI	Sinopharm	AstraZeneca	Pfizer	LSD
20–29	19.19 ± 4.11[a]	13.07 ± 2.02[a]	13.87 ± 4.05[a]	51.89 ± 14.24[b]	21.5
30–39	29.78 ± 7.51	19.22 ± 4.75	19.27 ± 5.97	16.09 ± 2.41	17.54
40–49	22.18 ± 8	29.38 ± 11.75	18.82 ± 7.81	32.39 ± 13.19	35.34
50–59	32.78 ± 9.5[a]	17.48 ± 1.72[b]	16.55 ± 3.29[b]	11.82 ± 4.86[b]	14.28

NI: Natural immunization via COVID-19 infection; similar letters indicate non-significant differences, while different letters indicate significant differences

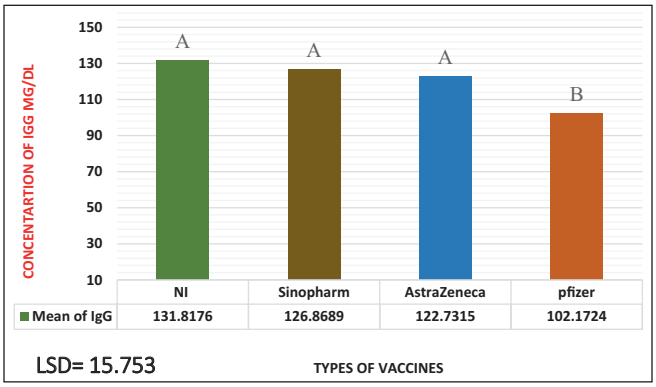

Figure 2: Comparing IgG concentration (mg/dL) between COVID-19 vaccinated individuals and unvaccinated (naturally infected) persons. Similar letters indicate non-significant differences, while different letters indicate significant differences

and those who were unvaccinated but infected with the virus, and it was found that unvaccinated individuals had a higher IgG concentration (131.8176 ± 4.64 mg/dL) compared to those who received the Pfizer vaccine (102.1724 ± 7.71 mg/dL) that had the less concentration with significant difference ($P < 0.05$). The Sinopharm and AstraZeneca vaccines had IgG levels of 126.8689 ± 5.90 and 122.7315 ± 3.15 mg/dL, respectively (that means the Sinopharm vaccine had the higher level of IgG than other covid-19 vaccines), which were slightly lower than unvaccinated individuals but significantly higher ($P < 0.05$) than those who received the Pfizer vaccine as shown in Figure 2.

IgG level between different COVID-19 vaccines and unvaccinated persons according to gender

The IgG concentration differences among males and females who received different COVID-19 vaccines and those who were unvaccinated but had been infected with the virus were presented in Table 3. The results showed that males who received the AstraZeneca vaccine had significantly higher IgG levels ($P < 0.05$) than females (127.87 ± 9.62 and 118.76 ± 6.33 mg/dL, respectively). On the other hand, females who received the Sinopharm vaccine had slightly higher levels of IgG compared to males (125.36 ± 4 and 124.27 ± 3.67 mg/dL, respectively) with no significant difference ($P > 0.05$), Which was similarly found in unvaccinated (naturally infected) females and males. In the case of the Pfizer vaccine, females had higher IgG levels than males (106.58 ± 10.35 and 97.39 ± 11.82 mg/dL, respectively) with significant differences ($P < 0.05$). Also, unvaccinated females had higher IgG levels than unvaccinated males (134.14 ± 6.25 and 128.85 ± 7.16 mg/dL, respectively) with a significant difference ($P < 0.05$).

The level of IgG according to the age groups

Table 4 shows that individuals aged 20–29 years who were unvaccinated but infected with the virus had the highest IgG levels (133.87 ± 6.33 mg/dL), while individuals who received the Pfizer vaccine had the lowest IgG levels (93.1 ± 13.49 mg/dL) with significant differences ($P < 0.05$). Individuals who received the Sinopharm vaccine had higher IgG levels (120.36 ± 11.68 mg/dL) than those who received the AstraZeneca vaccine (115.02 ± 4.99 mg/dL).

For individuals aged 30–39 years, the individuals that had the Sinopharm vaccine had higher IgG levels (136.12 ± 7.32 mg/dL) compared to those who received the Pfizer vaccine, which was lower in IgG level (109.29 ± 19.96 mg/dL) with significant differences ($P < 0.05$). Unvaccinated (infected) people had IgG levels (125.5 ± 15.82 mg/dL) that were lower than those who received Sinopharm and AstraZeneca vaccines (136.12 ± 7.32 and 134.6 ± 8.61 mg/dL, respectively) and higher than those who received the Pfizer vaccine (109.29 ± 19.96 mg/dL) with significant differences ($P < 0.05$). The LSD value for this age group was 41.69.

The 40–49 age group, who received the Sinopharm vaccine, had higher IgG levels (134.57 ± 6.32 mg/dL), while those who received the Pfizer vaccine had lower IgG levels (99.07 ± 16.55 mg/dL) with significant differences ($P < 0.05$). In contrast, the unvaccinated but infected had higher IgG levels (130.13 ± 4.7 mg/dL) than individuals that had the AstraZeneca vaccine (129.7 ± 4.1 mg/dL) and significantly higher ($P < 0.05$) than Pfizer vaccine but lower than individuals that received the Sinopharm vaccine (134.57 ± 6.32 mg/dL) with no significant differences ($P > 0.05$).

Table 3: IgG levels (mg/dL) in vaccinated individuals with COVID-19 vaccines and unvaccinated (naturally infected) persons by gender

Type of vaccine	Group		
	Males	Females	*P* value)
AstraZeneca	127.87 ± 9.62[a]	118.76 ± 6.33[a]	0.932
Sinopharm	124.27 ± 3.67[a]	125.36 ± 4[a]	0.217
Pfizer	97.39 ± 11.82[a]	106.58 ± 10.35[a]	0.447
Natural immunization	128.85 ± 7.16[a]	134.14 ± 6.25[a]	0.934

NI: Natural immunization via COVID-19 infection; similar letters indicate non-significant differences, while different letters indicate significant differences

Table 4: IgG levels (mg/dL) among different types of COVID-19 vaccines and unvaccinated individuals (naturally infected) according to age groups

Groups of age (years)	Type of vaccine				
	NI	Sinopharm	AstraZeneca	Pfizer	LSD
20–29	133.87 ± 6.33[a]	120.36 ± 11.68[a]	115.02 ± 4.99[a]	93.1 ± 13.49[b]	27.36
30–39	125.5 ± 15.82	136.12 ± 7.32	134.6 ± 8.61	109.29 ± 19.96	41.69
40–49	130.13 ± 4.7[a]	134.57 ± 6.32[a]	129.7 ± 4.1[a]	99.07 ± 16.55[b]	30.05
50–59	134.44 ± 5.92	127.09 ± 3.92	121.98 ± 5.64	120.4 ± 7.53	19.93

NI: Natural immunization via COVID-19 infection; similar letters indicate non-significant differences, while different letters indicate significant differences

Lastly, for individuals aged 50-59, unvaccinated individuals who had been infected with the virus had significantly higher IgG levels (134.44 ± 5.92 mg/dL) compared to those who received the Pfizer vaccine that had less IgG levels (120.4 ± 7.53 mg/dL) with significant differences ($P < 0.05$). The Sinopharm vaccine was higher than the AstraZeneca vaccine in the IgG level (127.09 ± 3.92 and 121.98 ± 5.64 mg/dL, respectively), and these vaccines are higher than the Pfizer vaccine with no significant differences ($P > 0.05$) but lower than unvaccinated(infected) people with significant differences ($P < 0.05$).

Discussion

The current study found that the Pfizer vaccine produces significantly higher $CD8^+$ levels compared to other COVID-19 vaccines and unvaccinated individuals. This observation emphasizes the effectiveness of mRNA vaccines in stimulating quick and functional responses from $CD8^+$ T-cells. The difference in $CD8^+$ levels between COVID-19 vaccines and unvaccinated individuals may be due to differences in viral antigen composition. The Pfizer vaccine, a type of nucleic acid vaccine (that contains mRNA incorporated with nanoparticles), works by incorporating genetic material into the host's antigen-presenting cell genome. This process can lead to the production of viral proteins within the cell, which are then presented on MHC class I molecules, leading to $CD8^+$ T-cell activation.[16] The vaccine also contains nanoparticles that are known to stimulate cellular immune responses, including $CD8^+$ T-cells.[17] The Pfizer vaccine was also found to induce a higher level of IFN-γ-producing $CD8^+$ T-cells in the bloodstream, specifically targeting the spike glycoprotein receptor binding domain, compared to individuals who have recovered from COVID-19.[18] Therefore, the Pfizer vaccine is more effective at triggering $CD8^+$ T-cell responses, thereby enhancing cellular immunity.

The second higher level of $CD8^+$ was observed in a group of a natural infection that induced high innate and adaptive immune response, but after the persistence of the virus in the host leading to T-cell exhaustion and the impairment of $CD4^+$ T-cells by COVID-19 leads to heightened activation and potential exhaustion of $CD8^+$ T-cells.[19] Sinopharm is an inactivated vaccine that contains killed coronavirus; this vaccine tends to induce more humoral responses than cellular immune responses.[20]

Also, the study showed that the AstraZeneca vaccine had a lower $CD8^+$ level. This may be due to the vaccine being found to have poor inducing of $CD8^+$ T-cells and due to containing adenovirus as a vector, which found these vectors have a tendency to persist at low levels and extend the duration of effector T-cell responses, leading to a delay in the transition of T-cells into a memory state and causes the overstimulation of type I interferons (IFNs) which leads to decreased expression of the transgene and diminished immune responses, both in terms of antibodies and cellular reactions.[21,22] The current study is compatible with a study by Fodor *et al.*[23] that also found the Pfizer vaccine produces a higher level of $CD8^+$ than other COVID-19 vaccines

and unvaccinated (naturally infected). According to another study, the overall T-cell response generated by the Sinopharm vaccine was lower (28.6%) than the T-cell response observed following the Pfizer vaccine (73–74%). In other words, the Pfizer vaccine generated a stronger T-cell response compared to the Sinopharm vaccine.[18]

This study also observed that unvaccinated (naturally infected) people, Pfizer and AstraZeneca vaccines, had higher levels of $CD8^+$ in males than females compared to the Sinopharm vaccine, which was more effective in females than males. This indicated the Pfizer and AstraZeneca vaccine's higher effectiveness in producing $CD8^+$ levels in males than females, while the Sinopharm vaccine was more effective in females. This is due to gender being an important factor that affects immune response against vaccines and detects their effectiveness.[24] A study found that males had higher levels of $CD8^+$ T-cell specific to the spike protein of SARS-CoV-2 following the Pfizer vaccine than females.[25] Also, research has shown that sex differences play a significant role in the variation of the immune response to COVID-19 in both innate and adaptive immune responses.[26]

The present study found that the Sinopharm vaccine and unvaccinated (naturally infected) people were more highly effective in $CD8^+$ levels in both 40–49 and 50–59 years age groups than other COVID-19 vaccines with significant differences. While the Pfizer vaccine was highly effective in 20–29 years and 30–39 years age groups with a significant difference ($P < 0.05$), it's lower effective in 50–59 years. This may be because the Sinopharm vaccine is more effective in those above 40 years of age than younger, while Pfizer vaccines are highly effective in younger than older individuals. This difference in the effectiveness of vaccines due to the immune response to vaccines is influenced by age, and age is a significant factor in determining their effectiveness.[24] Another study revealed that the T-cell response to the Sinopharm vaccine was less effective in older individuals. Although this difference was not statistically significant, the study suggests that younger individuals (20–39 years old) were more likely to have a functional T-cell response than older individuals.[27]

The level of IgG was found in this study to be significantly higher ($P < 0.05$) in the unvaccinated (naturally infected) people than in COVID-19 vaccines. Also, the Sinopharm vaccine had a higher level of IgG, while the Pfizer vaccine had a lower level. This variation in immune response due to the difference in viral antigen components of the vaccines and depended on it determined the type of immune response. Natural infection is more effective in inducing a humoral immune response than vaccines because, after SARS-CoV-2 infection, there is a sudden activation of B cells, producing virus-specific IgM, IgG, and IgA antibodies.[19] Additionally, the number of memory B cells specific to the spike protein increases over time after the onset of symptoms.

In contrast, the levels of SARS-CoV-specific $CD4^+$ T-cells and $CD8^+$ T-cells decline with a half-life of 3 to 5 months.[19] Consequently, natural infection provides immunity of considerable duration because memory B cells can promptly respond to reinfection by generating new plasma cells with high affinity, which is crucial for establishing long-lasting immunity.[19,28] Meanwhile, the Sinopharm vaccine primarily elicits an immune response focused on the production of antibodies.[20] After receiving the inactivated vaccine, rapid antibody responses targeting SARS-CoV-2 were observed.[29] This may be because the viral antigens in the inactivated whole-virion formulation can be directly presented to DCs through the lysosomal pathway and then activate the Th2 cell, which activates the humoral immune response.[19] On the other hand, this vaccine is poor in inducing cellular immunity.

In contrast, the AstraZeneca vaccine contains an adeno vector that causes poor inducing humoral by causing the overstimulation of type I interferons (IFNs), which leads to decreased expression of the transgene and weakened immune responses, both in terms of antibodies and cellular reactions.[22] The Pfizer vaccine has shown a tendency to generate durable and long-lasting protection of CD8+ T-cells against SARS-CoV-2. In contrast, the antibody-mediated response appears to diminish over time.[30] This decline in antibody levels following vaccination has been hypothesized to be influenced by plasma blasts that fail to develop into long-lived memory plasma cells.[31] Furthermore, the Pfizer vaccine, being a genetic vaccine and containing nanoparticles, has a propensity to elicit a stronger cellular response rather than a predominantly humoral response.[16,17]

The present study was compatible with a study that reported after receiving the second dose of the Sinopharm vaccine, 95.07% of individuals had detectable levels of SARS-CoV-2 specific total antibodies three months later. This suggests that the vaccine is effective in generating a robust immune response against the virus.[27] A study found that after receiving mRNA COVID-19 vaccines, individuals gradually decreased their antibody levels over a span of 4–6 months post-vaccination.[32] Research revealed that the levels of S- and RBD-specific IgG antibodies were considerably higher in individuals who had recovered from COVID-19 and tested negative for SARS-CoV-2, and they suggest that antibodies may have a critical role in eliminating the virus from the body.[33] However, the duration and levels of antibody response can vary among individuals and may depend on several factors, such as the severity of the infection, age, and underlying health conditions.[19]

Also, the current study found that for unvaccinated (naturally infected) people, Sinopharm and Pfizer's vaccines were generating a higher level of IgG level in females than males, while the AstraZeneca vaccine was found to generate a higher level of IgG in males than females. Perhaps this is due to Sinopharm and Pfizer vaccine's higher effectiveness inducing a humoral immune response in females than in males, while the AstraZeneca vaccine was more active in males. This may be due to differences in the effectiveness of immune responses between the two genders, as mentioned by the World Health Organization (WHO), which has reported that when it comes to immune responses to viral vaccines, men and women show differences.[24] In particular, women tend to develop significantly higher levels of humoral immunity compared to men, and also noted that females generally exhibit stronger cellular and humoral immune responses to infections, antigenic stimulation, and vaccination compared to males.[34] A study found that female patients had a stronger production of IgG antibodies against SARS-CoV-2 three months after being discharged.[35]

This study demonstrated that unvaccinated (naturally infected) individuals had a higher level of IgG in both the 20–29 years and 50–59 years age groups than covid19 vaccines, while the Sinopharm vaccine had a higher IgG level in both 30–39 years and 40–49 years age groups than other COVID-19 vaccines and unvaccinated (infected) individuals. Also found that the AstraZeneca vaccine had the same Sinopharm vaccine that was high in both the 30–39 years and 40–49 years age groups and lower in both the 20–29 years and 50–59 years age groups but was lower effective than the Sinpharm vaccine. This may be due to natural infection inducing a robust humoral immune response in the 20–29 years and 50–59 years age groups, while the Sinopharm vaccine is highly active to induce a humoral immune response in the 30–39 years and 40–49 years age groups. This difference may be due to the immune response to vaccines affected by age.[24] A study by Li *et al.*[33] found that older patients (unvaccinated) with more severe diseases had significantly higher levels of IgG antibodies, suggesting that these patients may experience stronger immune system activation during recovery. A study that looked at IgG anti-RBD antibodies in people with the Sinopharm vaccine found higher levels of IgG in people under 50 years old than above 50 years old at 8 weeks after vaccination.[36] According to this study, the levels of antibodies produced after receiving the Sinopharm vaccine decreased significantly as age increased. In other words, older individuals had lower antibody levels than younger individuals who received the same vaccine.[27]

Conclusion

In conclusion, the Pfizer vaccine showed significantly higher $CD8^+$ levels by inducing a cellular immune response. Natural immunization had higher IgG by inducing a humoral immune response than COVID-19 vaccines. These findings highlight the variability in immune responses elicited by different viral antigen compositions, which can also be influenced by factors such as gender and age.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Hu B, Guo H, Zhou P, Shi ZL. Characteristics of SARS-CoV-2 and COVID-19. Nat Rev Microbiol 2021;19:141-54.
2. Parasher A. COVID-19: Current understanding of its pathophysiology, clinical presentation, and treatment. Postgrad Med J 2021;97:312-20.
3. Song Z, Xu Y, Bao L, Zhang L, Yu P, Qu Y, *et al*. From SARS to MERS, thrusting coronaviruses into the spotlight. Viruses 2019;11.
4. Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC. Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): A review. JAMA 2020;324:782-93.
5. Marei HE, Althani A, Afifi N, Pozzoli G, Caceci T, Angelini F, *et al*. Pandemic COVID-19 caused by SARS-CoV-2: Genetic structure, vaccination, and therapeutic approaches. Mol Biol Rep 2021;48:6513-24.
6. Al-Kaif LA, Al-Saadi MA, Al-Charrakh AH. Effect of SARS-CoV-2 infection on HBV-infected patients: Reactivation. Med J Babylon 2022;19:736-46.
7. Wang C, Zhou X, Wang M, Chen X. The impact of SARS-CoV-2 on the human immune system and microbiome. Infect Microbes Dis 2021;3:14-21.
8. Manan A, Pirzada RH, Haseeb M, Choi S. Toll-like receptor mediation in SARS-CoV-2: A therapeutic approach. Int J Mol Sci 2022;23:10716.
9. Kumar S, Nyodu R, Maurya VK, Saxena SK. Host immune response and immunobiology of human SARS-CoV-2 infection. Coronavirus Disease 2019 (COVID-19) 2020:43-53.
10. Saad N, Moussa S. Immune response to COVID-19 infection: A double-edged sword. Immunol Med 2021;44:187-96.
11. Gupta SL, Jaiswal RK. Neutralizing antibody: A savior in the COVID-19 disease. Mol Biol Rep 2022;49:2465-74.
12. Xia Y, Yao RQ, Zhao PY, *et al*. Publication trends of research on COVID-19 and host immune response: A bibliometric analysis. Front Public Heal 2022;10:1-14.
13. Teijaro JR, Farber DL. COVID-19 vaccines: Modes of immune activation and future challenges. Nat Rev Immunol 2021;21:195-7.
14. Smatti MK, Alkhatib HA, Thani AAA, Yassine HM. Will host genetics affect the response to SARS-CoV-2 vaccines? Historical precedents. Front Med (Lausanne) 2022;9:802312.
15. Rosa-Fraile M, Sampedro A, Rodríguez-Granger J, Camacho E, Manrique E. Suitability of frozen serum stored in gel separator primary sampling tubes for serological testing. Clin Diagn Lab Immunol 2004;11:219-21.
16. Beijnen EMS, van Haren SD. Vaccine-induced CD8+ T cell responses in children: A review of age-specific molecular determinants contributing to antigen cross-presentation. Front Immunol 2020;11:1-17.
17. Nooraei S, Sarkar Lotfabadi A, Akbarzadehmoallemkolaei M, Rezaei N. Immunogenicity of different types of adjuvants and nano-adjuvants in veterinary vaccines: A comprehensive review. Vaccines 2023;11:453-20.

18. Rapaka RR, Cross AS, McArthur MA. Using adjuvants to drive T cell responses for next-generation infectious disease vaccines. Vaccines 2021;9:820.
19. Kamińska D, Dęborska-Materkowska D, Kościelska-Kasprzak K, Mazanowska O, Remiorz A, Poznański P, *et al*. Immunity after COVID-19 recovery and vaccination: Similarities and differences. Vaccines 2022;10:1068-28.
20. Wodi AP, Valerie Morelli B. Principles of vaccination. Equine Clin Immunol 2021:263-78.
21. Hasanpourghadi M, Novikov M, Ambrose R, Chekaoui A, Newman D, Zhou XY, *et al*. T cell responses to adenoviral vectors expressing the SARS-CoV-2 nucleoprotein. Curr Trends Microbiol 2021;15:1-28.
22. McCann N, O'Connor D, Lambe T, Pollard AJ. Viral vector vaccines. Curr Opin Immunol 2022;77:102210.
23. Fodor E, Calvo IO, Kuten-Pella O, *et al*. Comparison of immune activation of the COVID vaccines: ChAdOx1, BNT162b2, mRNA-1273, BBIBP-CorV, and Gam-COVID-Vac from serological human samples in Hungary showed higher protection after mRNA-based immunization. Eur Rev Med Pharmacol Sci 2022;26:5297-306.
24. Zimmermann P, Curtis N. Factors that influence the immune response to vaccination. Clin Microbiol Rev 2019;32:e00084-18.
25. Bai J, Chiba A, Murayama G, Kuga T, Tamura N, Miyake S. Sex, age, and ethnic background shape adaptive immune responses induced by the SARS-CoV-2 mRNA vaccine. Front Immunol 2022;13:1-14.
26. Yu C, Littleton S, Giroux NS, Mathew R, Ding S, Kalnitsky J, *et al*. Mucosal-associated invariant T-cell responses differ by sex in COVID-19. Medicine 2021;2:755-772.e5.
27. Jeewandara C, Aberathna IS, Pushpakumara PD, *et al*. Persistence of immune responses to the Sinopharm/BBIBP-CorV vaccine. Immun Inflamm Dis. 2022;10:1-11.
28. Tang PCH, Ng WH, King NJC, Mahalingam S. Can live-attenuated SARS-CoV-2 vaccine contribute to stopping the pandemic? PLoS Pathog 2022;18:e1010821-7.
29. Zou S, Wu M, Ming F, Wu S, Guo W, Marley G, *et al*. Immune response and safety to inactivated COVID-19 vaccine: A comparison between people living with HIV and HIV – naive individuals. AIDS Res Ther 2022;19:1-8.
30. Shi Y, Huang J, Liu Y, Liu J, Guo X, Li J, *et al*. Structural and biochemical characteristics of mRNA nanoparticles determine anti-SARS-CoV-2 humoral and cellular immune responses. Sci Adv 2022;8:1-14.
31. Föhse FK, Geckin B, Martijin Z. The impact of BNT162b2 mRNA vaccine on adaptive and innate immune responses. Clin Immunol 2023;255:109762.
32. Samanovic MI, Oom AL, Cornelius AR, Gray-Gaillard SL, Karmacharya T, Tuen M, *et al*. Vaccine-acquired SARS-CoV-2 immunity versus infection-acquired immunity: A comparison of three COVID-19 vaccines. Vaccines 2022;10:2152.
33. Li K, Huang B, Wu M, *et al*. Dynamic changes in anti-SARS-CoV-2 antibodies during SARS-CoV-2 infection and recovery from COVID-19. Nat Commun 2020;11.
34. Al-asadi AB, Al-nuaimi BN, Abdul-ghani MN, Al-maadhidi JF. Immune response among different types of SARS-CoV-2 vaccines in Iraq. J Commune Dis 2022:103-8.
35. Zhao YM, Shang YM, Song WB, Li Q-Q, Xie H, Xu Q-F, *et al*. Follow-up study of the pulmonary function and related physiological characteristics of COVID-19 survivors three months after recovery. EClinicalMedicine 2020;25:100463.
36. Hasan Z, Masood K, Qaiser S, Al E. BBIBP-CorV (Sinopharm) vaccination-induced immunity is affected by age, gender, and prior COVID-19 and activates responses to spike and other antigens. bioRxiv 8633;2022:30-51.