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Serum level of IgM and IgG in Responses to COVID-19 Vaccination in Iraq

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Abstract

The COVID-19 is pandemic disease, caused by the novel coronavirus SARS-CoV-2. It has enhanced extensive research about the immune responses of infection and vaccination. This study aimed to measurement of serum antibodies (IgM and IgG) levels in vaccinated individuals in Iraqi patients, and compares the responses between unvaccinated, Pfizer-vaccinated, Sinopharm-vaccinated, and COVID-19-infected groups. A total of 300 participants were categorized into four subgroups: 30 non-vaccinated and uninfected, 90 Pfizer-vaccinated, 90 Sinopharm-vaccinated after the second dose, and 90 COVID-19 infected, which assessed immune responses to Pfizer and Sinopharm COVID-19 vaccines over the first three months post-vaccination. IgM levels were significantly elevated in both the Sinopharm and Pfizer vaccine groups compared to the control group. Specifically, Sinopharm recipients had IgM levels of 5.33 ± 2.1 ng/ml, Pfizer recipients had 3.61 ± 1.14 ng/ml, and the control group had 0.6 ± 1.14 ng/ml. Notably, there were no significant differences in IgM levels between the Sinopharm and Pfizer groups. IgM levels in both Sinopharm and Pfizer groups slightly increased after the third month of vaccination. Sinopharm recipients exhibited a slight rise to 2.1 ± 0.7 ng/ml, while Pfizer recipients had a slight increase to 1.0 ± 0.3 ng/ml. IgG levels were significantly higher in the Pfizer vaccine group compared to the Sinopharm group and the control group. Pfizer recipients had a serum IgG level of 78.4 ± 12.3 ng/ml, followed by Sinopharm recipients at 68.4 ± 9.10 ng/ml, and the control group at 0.71 ± 0.02 ng/ml. After the third month of vaccination, both Sinopharm and Pfizer groups showed a decline in IgG levels. However, the Pfizer group maintained a higher level, with 50.2 ± 9.8 ng/ml compared to the Sinopharm group's 32.1 ± 5.4 ng/ml. These findings underscore the distinct immune responses elicited by different vaccines, providing valuable information for optimizing COVID-19 vaccination programs.

Keywords: COVID-19, IgM, IgG, Pfizer, Sinopharm.

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Introduction

A modified virus called SARS-CoV2 is the source of the Coronavirus Disease (COVID-19). The virus was discovered for the first time in December 2019 in Wuhan, China[1]. Three vaccines have been globally administered in Iraq: the Pfizer vaccine (is made from messenger RNA (mRNA) that has been engineered to encode the SARS-CoV-2 spike protein (S)), the Oxford AstraZeneca vaccine (employs a modified chimpanzee DNA adenovirus), and the Sinopharm vaccine (contains the inactivated SARS-CoV-2 virus)[2]. Despite the different modes of action of the COVID-19 vaccines, all of them target the spike protein because of its vital function[3].SARS-CoV-2's spike (S) protein is essential to infection by attaching itself to the ACE-2 receptor on host cells, it functions as a key, allowing the virus to fuse and enter[4]. Immunological markers, particularly immunoglobulin G (IgG) levels, are useful tools for evaluating the efficacy of virus vaccinations, because IgG represents the body's long-term humoral immune response[5]. IgG antibodies take longer to develop but provide more persistent protection than IgM antibodies, which are first produced by the immune system in response to a novel infection, including viruses. Consequently, after vaccination, higher IgG than IgM antibody levels suggest a stronger immunological response and possibly higher vaccine efficacy[6]. A SARS-CoV-2 infection can cause IgM antibodies to appear as early as 4 days after infection and to peak at roughly 20 days following, but IgG antibodies rise approximately 7 days after infection and reach their peak at about 25 days[7,8]. Conversely, serum may already have significant levels of IgG against SARS-CoV-2, which may be found alongside or ahead of IgM. Another study found that the levels of IgG and IgM specific to the SARS-CoV-2 virus peaked 17–19 days and 20–22 days after the onset of symptoms, respectively. Several types of seroconversions have been reported: IgG and IgM seroconversion concurrently, IgM seroconversion prior to IgG, and IgM seroconversion subsequent to IgG[9].

Studies on the immune response to SARS-CoV-2 after spontaneous infection have revealed that convalescent COVID-19 patients have IgG antibodies for several months after the onset of symptoms, though these antibodies capacity to neutralize the virus gradually deteriorates[10]. For the adaptive immune response to be effective against the SARS-CoV-2 immunoglobulins IgG and IgM are indispensable. IgG mainly works by neutralizing the virus, blocking its entrance into cells, and stimulating immune cells to destroy infected cells. The first immune response, IgM, on the other hand, helps to activate B cells so they can produce more IgG[11].

Assessing IgG and IgM levels after vaccination or infection is crucial for evaluating vaccine efficacy, determining the duration of protective immunity, and advancing the development of novel therapeutic approaches[12].

Materials and Methods

Subject:

There were Three hundred Iraqis that participated in this study. The participants were divided into four subgroups: thirty people were ranged from 24 to 35 (male equal to female), who were not vaccinated and uninfected, ninety people who received the Pfizer vaccine, ninety people who received the Sinopharm vaccine following the second dose of vaccination, and ninety people who were infected with COVID-19 but had not received the vaccine. The observation period was for the first three months after vaccination or

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infection. The ages of the vaccinated and infected groups varied from (25 to 40) years. Each of these groupings was then divided into three categories based on the length of vaccination or infection:

one month, two months, and three months. Between October 2021 and January 2022, medical professionals oversaw the collection of contaminated samples from Baghdad Teaching Hospital and Ibn Al-Kateeb Hospital in Baghdad, Iraq

Estimation Serum Level of IgM and IgG

Serum samples were obtained from all participants. Anti-SARS-CoV-2 IgM and IgG levels were quantified using Sunglong, China ELISA kits.

Statistical analysis:

The data analysis tools used were GraphPad Prism 9 and SPSS version 23. The mean, standard deviation, ANOVA, and ROC curves were among the statistical tests used.

Results and Discussion

Evaluation of Anti-S covid-19 immunoglobulin M (IgM) in the infected and vaccinated group:

Compared to the controls (0.6±0.01 ng/ml) and vaccinated groups, the follow-up data analysis revealed a significantly higher serum level of IgM in hospitalized patients after one month of infection (14.3±2.8 ng/ml). Following the first month of vaccination, the IgM levels were substantially higher in the Sinopharm vaccinate (5.33±2.1 ng/ml) and Pfizer vaccinate (3.61±1.14 ng/ml) groups than in the control group. However, no significant differences were observed within the vaccinated groups.

In comparison to the control group, the infected group exhibited a significantly higher IgM level (7.3±2.8 ng/ml) and Sinopharm vaccinate (3.9±1.3 ng/ml) in the second month following infection and vaccination, respectively. However, no significant differences were observed within the vaccinated groups. Pfizer vaccinate did not exhibit any significant differences in comparison to controls (1.4±0.6 ng/ml), respectively.

Compared to controls (0.6±0.01 ng/ml) and vaccinated groups, the IgM levels in patient (3.2±1.1ng/ml) and Sinopharm (2.1±0.7 ng/ml) and Pfizer (1.0±0.3 ng/ml) were slightly higher after the third month of infection and vaccination, as demonstrated in (figure 1).

Anti-S COVID-19 Immunoglobulin G (IgG) in the infected and vaccinated group: The data analysis showed that the infected group had a greater level of IgG identified in the first three months after infection and vaccination, and that after one month, the amount of serum IgG was higher (114.3±13.6 ng/ml). Compared to the controls (0.71±0.02 ng/ml), the Pfizer vaccinates had a higher serum IgG level (78.4±12.3 ng/ml), followed by the Sinopharm vaccinates (68.4±9.10 ng/ml).

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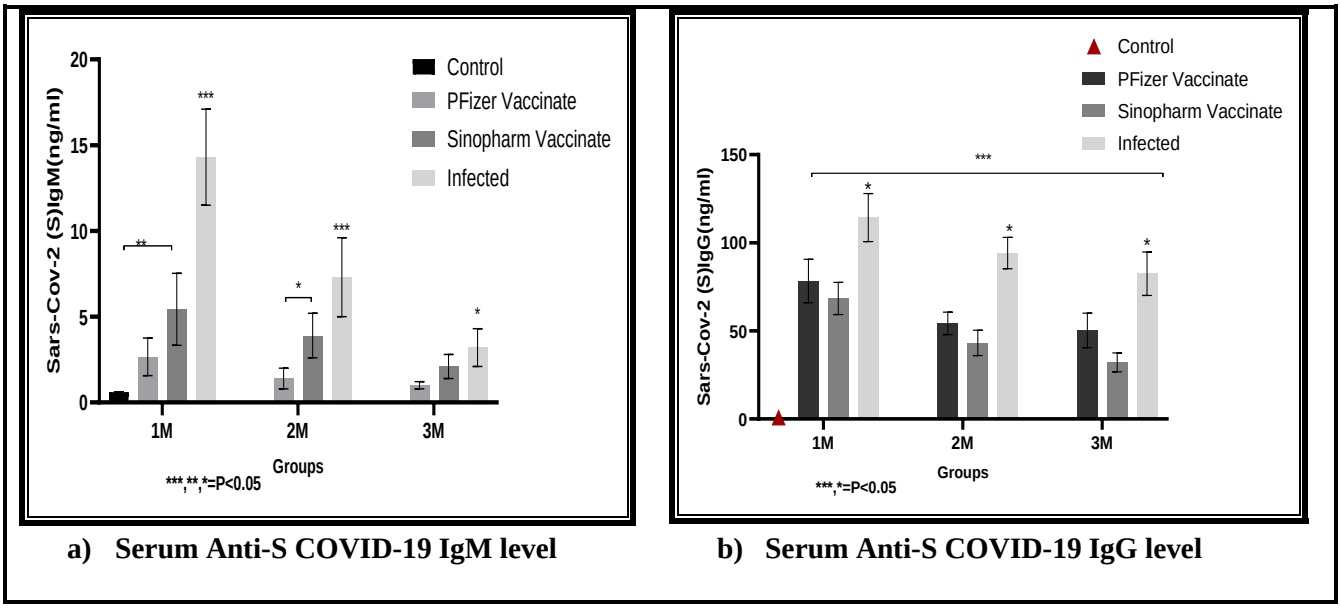
The second month after infection and vaccination showed notable variations as well. The IgG levels in the infected groups were substantially higher (94.2±8.9 ng/ml) than in the Sinopharm group (43.2±7.2 ng/ml), Pfizer vaccinated group (54.2±6.4 ng/ml), and control groups ($p<0.05$). The immunization group did not differ significantly from one another, nevertheless ($p>0.05$).

In comparison to the Pfizer (50.2±9.8 ng/ml) and Sinopharm (32.1±5.4 ng/ml) groups, as well as the control group (0.71±0.02 ng/ml), the infected groups also showed a considerable increase in the third month (82.4±12.3 ng/ml). However, as shown in (figure 1), no notable variations were found within the previously indicated categories.



a) Serum Anti-S COVID-19 IgM level **b) Serum Anti-S COVID-19 IgG level**

Figure 1. a) IgM and b) IgG serum levels in the infected and vaccinated groups.

One month after infection, higher serum levels of IgM were found in hospitalized patients compared to both the control and vaccinated groups. This finding emphasizes the immediate immunological response to SARS-CoV-2 pneumonia. The study's findings which support the findings of[13,14], showed that IgM levels are rising quickly. They observed that IgM antibodies against SARS-CoV-2 could be found within days of infection, peaking approximately three weeks later. Interestingly, the differential IgM response among vaccinated individuals, with Sinopharm recipients showing the highest levels followed by Pfizer, suggests vaccine-specific immune activation profiles. This phenomenon can be attributed to varying vaccine platforms and adjuvants used, affecting the immunogenicity and efficiency of the immune response[15].

Results showed a significant rise in IgG levels following vaccination and infection, indicating the beginning of a more robust immune response. In the first month after vaccination and infection, the infected group had the greatest IgG levels; thereafter, the Pfizer and Sinopharm vaccines showed significant increases in IgG levels. These outcomes are consistent with[16], who reported the presence of immunoglobulin G in high quantities in the post-infection period.

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Results are also in line with the study by[17], who demonstrated that IgG antibody levels in fully vaccinated individuals with the Pfizer-BioNTech vaccine exhibited higher quantitative efficiency compared to those who received the Sinopharm vaccine. Both immunizations produce S protein IgG and NAbs over a period of several months. They also show a modest TH2 response and a robust T helper (TH) 1 response.

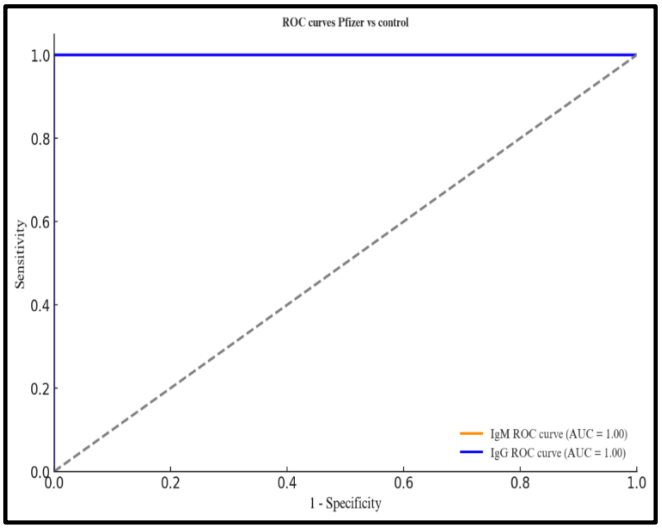
The weeks following vaccination, the anti-spike IgG concentration for the Pfizer vaccination varied greatly; as the weeks pass, the concentration rises, reaching its maximum between the sixth and seventh weeks and its lowest between the tenth and subsequent weeks, as demonstrated in[18].

ROC test Analysis:

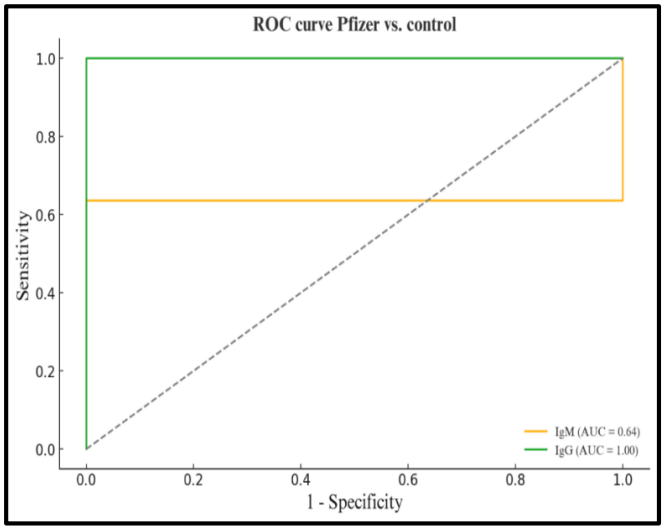
The Roc curve analysis of the Pfizer vaccine for IgM and IgG during the first month demonstrated (Sensitivity 100%, Specificity 100%, AUC: 1), while the analysis in third month demonstrated that IgM (Sensitivity 63.6 %, Specificity 63.6 %, AUC: 0.64 ± 0.10), and the IgG (Sensitivity 100%, Specificity 100%, AUC: 1.00 ± 0.00). This is shown in fig 2.

The Sinopharm vaccine, during the first month the ROC curve analysis for IgM and IgG showed higher sensitivity and specificity (Sensitivity 100%, Specificity 100%, AUC: 1), while in the third month the result for IgM yielded (Sensitivity 100%, Specificity 36.364%, AUC: 1.00 ± 0.10), and the IgG yielded (Sensitivity %: 100, Specificity %: 18.182, AUC: 1.00 ± 0.00) as shown in fig 3.

ROC analysis of the infected individual recorded in the first and the third months that IgM (Sensitivity 100%, Specificity 100%, AUC: 1.00±0.00) ROC analysis recorded that IgG (Sensitivity 100%, Specificity 100%, AUC 1.00±0.00) as shown in fig 4



a) ROC test of IgM and IgG after the first month



b) ROC test of IgM and IgG after the third month

Figure 2. Roc test of IgM and IgG after Pfizer vaccination

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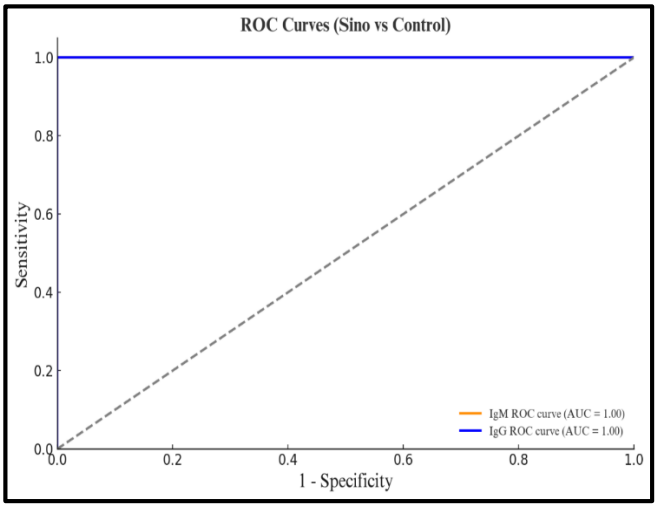
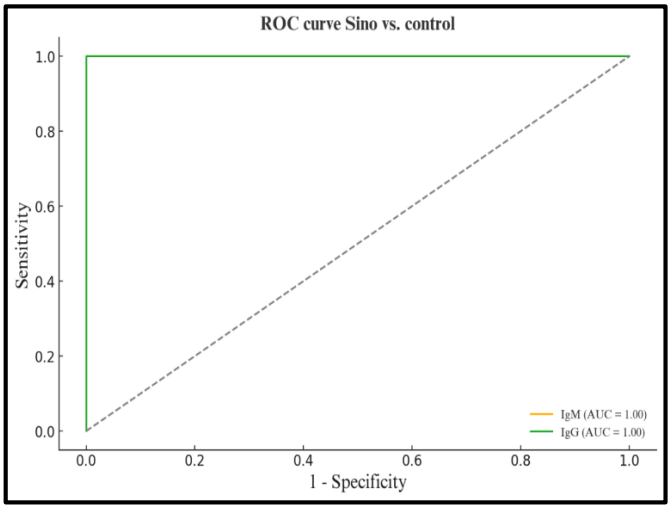
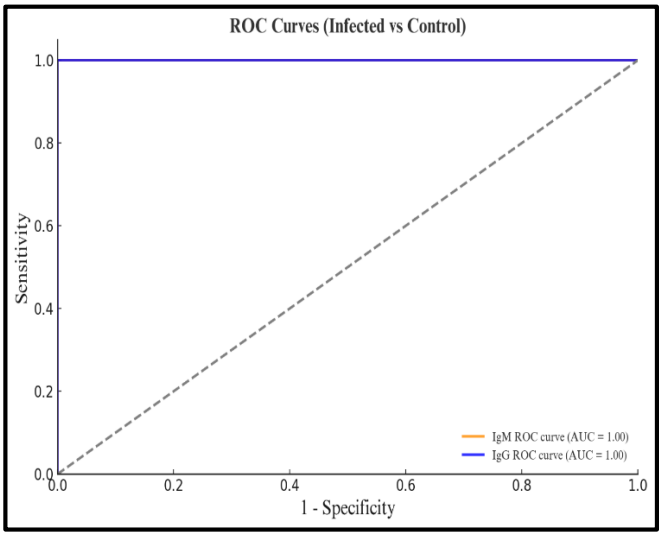


a) ROC test of IgM and IgG after the first month

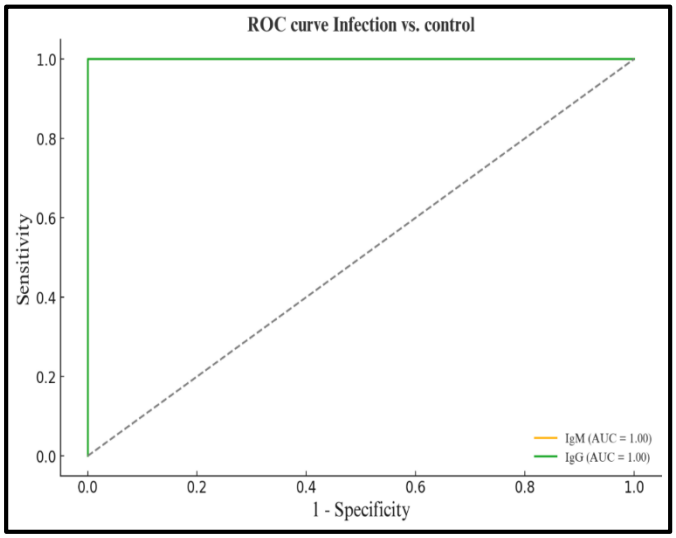


b) ROC test of IgM and IgG after the third month

Figure 3. Roc test of IgM and IgG after Sinopharm vaccination



a) ROC test of IgM and IgG after the first month



b) ROC test of IgM and IgG after the third month

Figure 4. Roc test of IgM and IgG after infection

A ROC analysis revealed that IgM and IgG levels are highly effective diagnostic markers for COVID-19 infection and the immune response to Pfizer and Sinopharm vaccines. IgM and IgG antibodies were identified as the most reliable indicators for assessing both infection status and vaccine efficacy.

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These markers demonstrated exceptional sensitivity and specificity of 100%, as well as high area under the curve (AUC) values, particularly within the first month after vaccination.

IgM levels exhibited a decline in sensitivity over time, especially in the third month following vaccination. In contrast, IgG levels maintained consistently high sensitivity and specificity throughout the study period. The superior diagnostic accuracy of IgG compared to IgM was further evidenced by the AUC (IgG) > AUC (IgM) result[19]. Additional research has demonstrated that SARS-CoV-2 serological testing can serve as a valuable adjunct to the current RT-PCR assay, enabling more accurate and timely identification of COVID-19 cases[20].

Overall, this investigation highlights the potential of utilizing various immunological markers to diagnose COVID-19 infection and assess vaccine response. The Pfizer vaccine group demonstrated superior diagnostic potential for both IgM and IgG compared to the Sinopharm group, which exhibited lower sensitivity and specificity values [21].

Conclusions

According to the study, the Pfizer vaccine induces high levels of IgM and IgG antibodies. IgG levels often reach their peak several weeks following the second dosage and stay there for three months, whereas the Sinopharm immunization tends to cause a quick reduction in antibody response.

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Author's Declaration

- We hereby confirm that all the Figures and Tables in the manuscript are original and have been created by us.
- We have obtained ethical clearance for our study from the local ethical committee at [Al-Nahrain University/College of Biotechnology]. This approval underscores our commitment to ethical research practices and the well-being of our participants.
- Ethical Clearance: The project was approved by the local ethical committee at [Al-Nahrain University/College of Biotechnology], ensuring adherence to ethical standards and the protection of participants' rights and welfare.

Author's Contribution Statement

[First Author's Name]: Played a critical role in the statistical analysis of the data and interpretation of the results.

[Second Author's Name]: Played a critical role in supervising the research, providing guidance, and designing the study

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