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Immediate Adverse Reaction and SARS-CoV-2 Anti-Spike Receptor Binding Domain IgG of COVID-19 Vaccines Among Health Staffs

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Original Research

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Abstract

Objective: To contain the spread of coronavirus disease 2019 (COVID-19), several vaccines have been developed. This study is intended to elucidate the level of anti-severe acute respiratory syndrome coronavirus 2 immunoglobulin G (anti-SARS-CoV-2-IgG) antibodies for COVID-19 vaccines (Pfizer BioNTech [BNT162b2], Oxford/AstraZeneca [ChAdOx1], and Sinopharm [BBIBP-CorV]) among health staff from health facilities in Duhok province, and it explored the immediate adverse reactions of COVID-19 vaccines among participants.

Methods: A longitudinal study was conducted from June 1, 2021, to June 30, 2022, and 300 participants were included through simple random sampling.

Results: The immune response 1 mo after the second dose was significantly higher than the sustained immune after 5 and 9 mo as results revealed that, in 100% of study samples who had (ChAdOx1) vaccine, their antibody titers exceeded the positivity threshold of 1 AU/m, while 96% for (BNT162b2) and 90% for (BBIBP-CorV) for the first test after 1 mo from the second dose of the COVID-19 vaccine, and these rates were reduced to 94.6% for (ChAdOx1), 97.8% for (BNT162b2), and 81.9% for (BBIBP-CorV) at 5 mo after the second dose, while simultaneously the seropositivity rates were more reduced at 9 mo to 46.5% for (ChAdOx1), 67.5% for (BNT162b2), and 9.20% for (BBIBP-CorV). In terms of adverse reactionsss, fever was reported as the most prevalent after the first dose in 58% for ChAdOx1, 43% for BNT162b2, and 23% for BBIBP-CorV, followed by muscle pain, joint pain, and shoulder pain for both doses.

Conclusions: The implications of the findings from this study are that higher and potentially longer antibody responses can be obtained if the BNT162b2 is given as compared with the other 2 vaccines. Moreover, the booster doses of the COVID-19 vaccine are highly recommended because more than 50% of the participants either have become anti-spike protein negative or have a deficient level of anti-spike protein against COVD-19 vaccines.

What do we already know about this topic? Coronavirus disease 2019 (COVID-19) vaccines have been developed and authorized for emergency use to protect against COVID-19, a highly contagious and potentially deadly disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus. The vaccines work by teaching the immune system to recognize and fight the virus, which can prevent illness or reduce the severity of symptoms. However, like all vaccines, COVID-19 vaccines can cause side effects, which can range from mild to severe. Some common side effects include pain or swelling at the injection site, fever, fatigue, headache, muscle aches, and chills.

Reports of more serious side effects, such as blood clots and heart inflammation, have also emerged, although these are rare. The risk of adverse reactions varies depending on the vaccine and the individual, and health authorities continue to monitor and investigate any safety concerns related to the vaccines

How does your research contribute to the field? Given this background, the research described in the title is focused on evaluating the level of SARS-CoV-2 anti-spike receptor binding domain (RBD) immunoglobulin G (IgG) of COVID-19 Vaccines prevalence and nature of adverse reactions specifically among health staff in Duhok Province, Iraq, who received COVID-19 vaccines.

What are your research's implications toward theory, practice, or policy? The results of this research could provide important insights into the safety and efficacy of COVID-19 vaccines, particularly among healthcare workers, and inform future vaccination policies and practices in the region.

Coronavirus disease is caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) known as COVID-19, which is a beta coronavirus that has emerged as 1 of the most contagious viruses in recent history.[1] Historically, coronaviruses have caused 3 major outbreaks in the past 2 decades: SARS (severe acute respiratory syndrome), MERS (Middle East

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respiratory syndrome), and the most recently emerged COVID-19.[2] The COVID-19 outbreak was first detected in the Wuhan province of China in December 2019.[3]

The World Health Organization (WHO) declared SARS-Cov-2 as a public health emergency on January 31, 2020. In addition, COVID-19 attained the status of a very high-risk category in February 2020 and was declared a pandemic in March 2020.[4] Globally, at the time of writing this study, there have been 533,816,957 confirmed cases of COVID-19, including 6,309,633 deaths. Contrarily, a total of 11,864,214,773 vaccine doses have been administered. Whereas, in Iraq, 2,330,049 confirmed cases and 25,223 deaths have been recorded, with a total of 18,353,783 vaccine doses having been administered.[5] A total of 15,409 cases were reported, particularly in Duhok in 2020.[6]

The wide spread of COVID-19 has affected numerous individuals' lives across the world and limited the movement of people outside their homes and territories. Many control measures were implemented to control the pandemic, such as movement restriction, social distancing, and wearing masks in crowded places, as well as a health education campaign to improve handwashing and avoid places where infections were likely. However, these precautionary measures were not able to control the pandemic, but they have resulted in a pandemic wave over time.[7]

Currently, the COVID-19 vaccine is 1 of the preventative strategies that could help to keep the pandemic under control. Many manufacturers created and delivered vaccines worldwide, including Pfizer and BioNTech, which introduced the first COVID-19 vaccine in December 2020. Even though the vaccinations provide a reasonable amount of protection against COVID-19 and reduce the mortality rate, their efficacy varies from 1 type of vaccine to another. Having mentioned that a high vaccination rate can end the COVID-19 pandemic, vaccination is being promoted globally.[8,9]

mRNA (BNT162b2 and mRNA-1273), adenoviral vector-based (ChAdOx1 nCoV-19, Ad26.CoV2.S, and Gam-COVID-Vac), and inactivated virus (CoronaVac and Sinopharm) vaccines are the most widely used vaccine types. Several studies have demonstrated the varying effectiveness of these vaccines. In phase 3 clinical trials, the BNT162b2 vaccine (from Pfizer and BioNTech) demonstrated 95% efficacy, whereas the ChAdOx1 vaccine (from the University of Oxford and AstraZeneca) demonstrated 74% efficacy.[10] The European Medicines Agency has authorized the use of both of these COVID-19 vaccines (BNT162b2 and ChAdOx1). Other countries carried out their own studies to explore the vaccine's efficacy. For example, Turkey reported an 83.5% efficacy for CoronaVac (from Sinovac), whereas Chile reported a 64.9% efficacy.[11,12] Meanwhile, the WHO approved the CoronaVac (from Sinovac) vaccine, assessing its efficacy at 51%. The reported differences in vaccine efficacy might be due to many reasons, including population differences or polymorphisms that were circulating in different places at the time. It is not clear and needs further research to find out the level of effectiveness of each vaccine and how long it protects people in the real world because all COVID-19 vaccines did not pass through a normal process for the normal vaccine development process, which usually takes 10-14 y, and there are new strains of the virus.

Antibodies serve as the initial line of defense during a natural COVID-19 infection, where their levels might be altered by factors such as illness severity and comorbidities. It is believed that antibodies against the SARS-CoV-2 spike protein, and specifically the RBD, play a crucial role in both stimulating the immune response and neutralizing the virus. Because the virus continues to spread and mutate, it is anticipated that immune-evasive forms may arise.[13,14] Studies have proven the necessity of high spike antibody titers to develop a protective immune response against SARS-CoV-2 infection. Studies have also shown a link between new infections and an increase in RBD IgG antibody titers. These results show that antibody titers are an important protective factor against SARS-CoV-2 infection.[15] While the vital role of vaccines is known to increase the level of the immune system, it is unknown how long the immunological response to the various vaccines will last and whether additional doses will be required.

Among the issues involved with vaccination is the possibility of adverse effects. COVID-19 vaccines were developed in record time to ensure that most of the population got vaccinated at the earliest time. Consequently, the side effects of vaccines have been seen among populations all over the world. The rate of adverse reactions to COVID-19 vaccinations varies by country because the kinds of vaccines administered vary as well. From mild to severe adverse reactions have been documented, including localized reactions like swelling, redness, and a rash at the injection site, as well as systemic reactions like dyspnea and anaphylaxis.[16] Due to the widespread misinformation and people's perceptions of adverse reactions to vaccines, many people choose not to get vaccines and avoid vaccination altogether. Low vaccination rates can impede the establishment of herd immunity at the level of the community.[17] The level of serum IgG is linked to the severity and length of adverse reactions to vaccines. People might be willing to get vaccinated and deal with the side effects if they know how their immune systems will react to COVID-19 vaccines over time and what kinds of side effects they might have. Clarifying the adverse reactions as per vaccine and individual characteristics are critical for mitigating the fear of COVID-19 vaccination and regaining a safer world with herd immunity. But there is not much known about the level of anti-SARS-CoV-2 IgG and the kinds of side effects of the COVID-19 vaccine at the moment. The way a person reacts to a vaccine depends on both the type of vaccine and the person.[18] Currently, Iraq has received different types of COVID-19 vaccines with no detailed efficacy data for these vaccines. However, the level of immunity to the 2019-nCoV vaccination and its lifetime in the community is unknown. Therefore, this research investigated the IgG level and adverse reactions to COVID-19 vaccines (ChAdOx1/AZD1222, BNT162b2, and BBIBP-CorV) among health-care workers over the course of a 9-mo period.

Methods

Study Design

A longitudinal study through the panel design was conducted to study the COVID-19 vaccines' stimulation to the immunity status as well as adverse side effects among staff in health-care facilities in Duhok province in Kurdistan region, Iraq. Participants of this study received 1 of the 3 available vaccines (Pfizer BioNTech [BNT162b2], Oxford/AstraZeneca [ChAdOx1], and Sinopharm [BBIBP-CorV]), and the time period for this study was between June 2021 and June 2022 for those who were working in public health-care facilities in Duhok Province, Iraq.

Participants

The study recruited 300 health staff from public health-care facilities in Duhok province, of which 300 participants were included in the first phase 1 mo after the second dose; 279 participants in the second

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phase 5 mo after the second dose; and 256 participants in the third phase of 9 mo after the second dose. Following inclusion criteria, the present study recruited health staff who received 2 doses of the COVID-19 vaccine. Vaccine types varied and included Pfizer BioNTech (BNT162b2), Oxford/AstraZeneca (ChAdOx1), and Sinopharm (BBIBP-CorV). Participants were included in this study if they gave consent and were willing to participate and commit to studying requirements. Contrary, people with cancer or human immunodeficiency virus (HIV) disease were excluded. The study sample was recruited using a vaccine database from the Duhok health governorate through a random sampling method. Initially, 904 healthcare workers who completed their vaccination by receiving 2 doses were recorded in the vaccination department and included in the original database for each vaccine. Then simple random sampling was performed using the Excel random formula to select 100 individuals for each vaccine to be included in the study.

Procedure

Blood collection was done between June 2021 and June 2022 in 4 places (Hevi hospital, Azadi teaching hospital, Directorate of preventive health affairs, and General Directorate of Health in Duhok, Iraq). For each round of sample collection, 3 ml of blood were taken from each participant, put in a tube, and put in the fridge. This was done so that there were 50 samples for each round of testing, because the Mini VIDAS machine could only test 50 samples at a time. SARS-CoV-2 anti-spike RBD IgG was then measured. The samples were tested in the public health central laboratory in Duhok province. The assay VIDAS SARS-CoV-2 IgG (Biomerieux SA) had European CE marking authorization. Per the assay's recommended definition, the positive anti-spike RBD IgG response in the study was defined as a test value of 1.0 index or more, and the reported assay specificity was 99.9% (from the package insert). Assays were run on the VIDAS Mini VIDAS System. A set of questions were also included in a questionnaire to collect data about sociodemographic information (eg, age, sex, level of education, job title, and year of service). Then a blood sample was collected from each participant after 1 mo, 5 mo, and 9 mo after the second dose of the vaccine to determine the immunity stimulation status. In addition, information on the immediate adverse reactions to COVID-19 vaccines was gathered.

Data Collection and Measurement

Interpretation of results for SARS-CoV-2 anti-spike RBD IgG antibody has been performed after the SARS-CoV-2 control results have been reviewed, determined, validated, and were acceptable following the description in Table 1.

Technique to Reduce Bias

In this study, certain procedures were taken to minimize the bias, such as using the same kits and machine for all tests over the 3 different times of test. One person took the sample for all participants, and 2 laboratory technicians worked on the entire test and procedure. In the meantime, simple random sampling was also used as another strong point.

Statistical Methods

The descriptive characteristics of the participants were presented using mean (SD) or number (percentage). The IgG level and participants' response to the COVID-19 vaccine were reported in mean (SD) and number (percentage). Positivity at mo 1, 5, and 9 among participants with different characteristics was analyzed using a Pearson chi-squared test (Fisher's exact or chi-squared test). Comparisons of IgG levels of COVID-19 vaccines between different time periods for each vaccine were examined using the Bonferroni correction test. Additionally, the comparisons of IgG antibody levels 1 mo after the second dose of the COVID-19 vaccine among different age groups and genders were conducted using a 1-way analysis of variance (ANOVA) and independent t-test, respectively. The significance level for differences was set at a *P*-value of less than 0.05. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS), Version 23.

Table 1. Interpretation of results

Output (AU/mL)	Interpretation	Description
< 1	Negative	The sample should be considered negative for the presence of anti-SARS-CoV-2-IgG antibodies
≥ 1	Positive	The sample should be considered positive for the presence of anti-SARS-CoV-2-IgG antibodies

Results

This study recruited 300 health staff from public health-care facilities in Duhok province. Slightly above half of the participants were female (51.7% female) from 21 to 72 y of age (*mean of age* = 30.33; *SD* = 8.53). Nearly half (47%) of the respondents were between 31 and 40 y old. Most of the participants had high education levels (49.3% had college degrees). Underweight as a single symptom was not observed among any participants, while overweight and obese were observed at 43.7% and 12%, respectively, as shown in Table 2.

To further explore the relationship between socio-demographic background and SARS-CoV-2 anti-spike RBD IgG antibody positivity after 1 mo from the second dose of the COVID-19 vaccine, we carried out chi-square analyses and the results showed that age, body mass index (BMI), and smoking status had a significant relationship with SARS-CoV-2 anti-spike RBD IgG antibody positivity. Contrarily, among other demographic backgrounds, gender showed no significant relationship. Regarding the level of SARS-CoV-2 anti-spike RBD IgG antibody, this study found that 90% of the samples exceeded the positivity threshold of more than 1 AU for SARS-CoV-2 anti-spike RBD IgG antibody positivity despite the background differences (Table 3).

In the second part of the study, participants were monitored for SARS-CoV-2 anti-spike RBD IgG antibodies over the course of 9 mo. Antibody titers were obtained from each participant after 1 mo, 5 mo, and 9 mo after the second dose of the COVID-19 vaccine for the 3 available types of vaccines. As shown in Table 4, the study showed that mean values of the SARS-CoV-2 anti-spike RBD IgG antibody were significantly decreased from 52.12 to 29.02 and 6.49 in 1, 5, and 9 mo, respectively ($P < 0.0001$). The overall difference was significant between mo 1 and mo 5 and 9, and between mo 5 and 9 (further detail in Figure 1).

This study also evaluated the level of SARS-CoV-2 anti-spike RBD IgG antibody among participants over 9 mo. As shown in Figure 2, the mean of SARS-CoV-2 anti-spike RBD IgG antibodies among the receivers of (BNT162b2) vaccine was higher over the

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Table 2. Socio-demographic profile of participants

Characteristic	Categories	Number (*N* = 300)	Percent
Sex	Female	155	51.7
	Male	145	48.3
Education level	Primary school	18	6
	Intermediate school	14	4.7
	High school	13	4.3
	Institute	92	30.7
	College	148	49.3
	Postgraduate	15	5
Profession	administrative staff	60	20
	Assistant nurse	37	12.3
	laboratories staff	36	12
	Nurse	79	26.3
	Pharmacist	14	4.7
	Physician	60	20
	Engineer	14	4.7
Age group	20-30 years	67	22.3
	31-40 years	141	47
	41-50 years	63	21
	51-60 years	24	8
	>60 years	5	1.7
BMI	Normal	133	44.3
	Overweight	131	43.7
	Obese	36	12
Smoking status	Not smoker	178	59.3
	Ex-smoker	34	11.3
	Active smoker	88	29.3
Alcohol status	Yes	35	11.7
	No	265	88.3
Total		300	100%

course of 1 mo, 5 mo, and 9 mo after the second dose compared with (ChAdOx1) and (BBIBP-CorV), which came in second and third place and statistically significant over the time ($P = 0.0001$), respectively.

Furthermore, after 1 mo from the second dose of COVID-19 vaccine receiver, the mean IgG level was found to be higher in younger people (mean 34 for < 60-y-olds) as compared to older people (mean = 22 for > 60-y-old) and was statistically significant at $P < 0.0084$, whereas sex had no significant association ($P = 0.7395$ and $P = 0.3948$) with the IgG levels against the RBD antibody over the 1 and 5 mo from the second dose of COVID-19 vaccine receiver while in mo 9, sex was significant association ($P = 0.0001$) with the IgG levels against the RBD antibody since the mean of female (mean = 3.45) was higher than the male (mean = 0.26). More details in Table 5.

The relationship between adverse effects and the type of vaccine received during the first 12 h to 1 mo after the first and second doses was also explored. The results showed that fever (58%) was the most prevalent after the first dose of the ChAdOx1, and (43% of participants had a fever for BNT162b2 and (23% for BBIBP-CorV), followed by muscle pain, joint pain, and shoulder pain for both doses. A list of the adverse reactions to the COVID-19 vaccine is shown in Table 6.

Regarding the uncommon adverse reactions following the COVID-19 vaccines, among participants who reported an adverse reaction, a small percentage also experienced uncommon reactions, including increased appetite change, sex activities, and monthly periods among female participants. More details are shown in Table 7.

Discussion

This study explored status of immunity for the COVID-19 vaccine among health-care workers through testing of the level of response of anti-SARS-CoV-2-IgG antibodies to the vaccine as well as information on adverse reactions, to know the vaccine's effectiveness SARS-CoV-2 anti-spike RBD IgG antibodies for 3 types of vaccines available vaccine in Iraq. We also analyzed the impacts of the socio-demographic variables on the SARS-CoV-2 anti-spike RBD IgG antibody. Furthermore, the study monitored the adverse reactions for each vaccine separately. This study showed that anti-spike RBD IgG antibodies varied among participants depending on the type and how much time passed from receiving the COVID-19 vaccines. For example, after 9 mo from the second dose, the SARS-CoV-2 anti-spike RBD IgG antibody positivity had decreased by more than 50% for all 3 types of vaccine. After 9 mo, SARS-CoV-2 anti-spike RBD IgG antibody positivity was higher in those who received the Pfizer vaccine compared with those who received the other types of COVID-19 vaccines.

The mean level of SARS-CoV-2 anti-spike RBD IgG antibody against 3 types of vaccines has been reduced by more than half from 1 mo compared with 9 mo after the second dose of vaccine since the highest mean with BNT162b2 (mean 47.3 to 6.7), followed by ChAdOx1 (mean 37.6 to 2.84), and lowest in the Sinopharm group (16.7 to 0.30), which is a similar finding to that reported by a study conducted in Greece.[19] Our results are also comparable with studies suggesting that the third dose of vaccine is necessary.[20] This study found that the peak antibody titers were observed 1 mo after the second dose, with the lowest positivity of SARS-CoV-2 anti-spike RBD IgG antibody observed 9 mo later.

Regarding sociodemographic impacts, this study revealed that there was an association between SARS-CoV-2 anti-spike RBD IgG antibody of the vaccine and recipients' age, BMI categories, and smoking status after receiving the 3 types of vaccines. Another study also reported that age may also play a role in immunity acquisition following COVID-19 vaccination.[21] This study revealed a correlation between age and anti-SARS-CoV-2 IgG levels, with younger people having greater IgG levels as compared to older people. As shown by previous studies,[22] this may be attributable to the fact that immunity is more viable in younger populations than in older populations. Younger people tend to have more T and B cells associated with adaptive immunity and active toll-like receptor reactions, which show a stronger correlation with higher IgG levels in younger individuals.[22]

Sex had no significant association with the IgG levels against RBD antibody for the month 1 and months 5 after second dose of COVID-19 vaccine, whereas in month 9, there was significant association which is similar to other study findings that females have significantly higher baseline levels of antibodies than males.[23]

Adverse reactions included redness at the injection site after the first dose and induration, heat, and swelling at the injection site, along with systemic symptoms, fever, and headache after the second dose.[22] Uncommon adverse reactions were also reported, such as increased appetites and better sex activity among Pfizer vaccinees, while loss of appetites and lower sex activity were reported among a group of people who got Sinopharm vaccines.

In terms of side effects, local and systemic adverse events after the first and second doses of vaccines were similar to other studies.

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Table 3. Distribution and association of SARS-CoV-2 anti-spike RBD IgG positivity level according to the demographic profile of participants after 1, 5, and 9 mo from the second dose of COVID-19 vaccines

	Positivity at mo 1 no (%)			Positivity at mo 5 no (%)			Positivity at mo 9 no (%)		
Characteristic (n = 300)	Positive	Negative	*P*-Value	Positive	Negative	*P*-Value	Positive	Negative	*P*-Value
COVID-19 vaccine			0.0002			0.0001			<.0001
AstraZeneca	100 (100.00)	0 (0.00)		87(94.57)	5(5.43)		40(46.51)	46(53.49)	
Pfizer	99 (99.00)	1 (1.00)		90(97.83)	2(2.17)		56(67.47)	27(32.53)	
Sinopharm	90 (90.00)	10 (10.00)		77(81.05)	18(18.95)		8(9.20)	79(90.80)	
Age group (y)			0.0003			0.0697			0.0006
20-30	67 (100.00)	0 (0.00)		61(98.39)	1(1.61)		34(61.82)	21(38.18)	
31-40	139 (98.58)	2 (1.42)		118(90.77)	12(9.23)		38(30.65)	86(69.35)	
41-50	59 (93.65)	4 (6.35)		51(87.93)	7(12.07)		18(36.00)	32(64.00)	
51-60	20 (83.33)	4 (16.67)		20(83.33)	4(16.67)		13(59.09)	9(40.91)	
>60	4 (80.00)	1 (20.00)		4(80.00)	1(20.00)		1(20.00)	4(80.00)	
Gender			0.8457			0.0821			0.9619
Female	149(96.13)	6(3.87)		127(88.19)	17(11.81)		53(40.77)	77(59.23)	
Male	140(96.55)	5(3.45)		127(94.07)	8(5.93)		51(40.48)	75(59.52)	
BMI			0.0323			0.8293			0.7023
Normal	132(99.25)	1(0.75)		114(91.94)	10(8.06)		49(43.36)	64(56.64)	
Overweight	123(93.89)	8(6.11)		109(90.83)	11(9.17)		43(39.09)	67(60.91)	
Obese	34(94.44)	2(5.56)		31(88.57)	4(11.43)		12(36.36)	21(63.64)	
Smoking status			0.0010			0.4260	63(42.86)	84(57.14)	0.6947
Not smoker	175(98.31)	3(1.69)		151(92.07)	13(7.93)		11(36.67)	19(63.33)	
Ex-smoker	29(85.29)	5(14.71)		27(84.38)	5(15.63)		30(37.97)	49(62.03)	
Active smoker	85(96.59)	3(3.41)		76(91.57)	7(8.43)		63(42.86)	84(57.14)	
Alcohol status			0.7863			0.1897			0.3608
Yes	34(97.14)	1(2.86)		33(97.06)	1(2.94)		11(33.33)	22(66.67)	
No	255(96.23)	10(3.77)		221(90.20)	24(9.80)		93(41.70)	130(58.30)	

Table 4. Mean of SARS-CoV-2 anti-spike RBD IgG antibody among health staff after 1, 5, and 9 mo from the second dose of COVID-19 vaccines

	Time period (mean)				
COVID-19 vaccine types	Mo 1	Mo 5	Mo 9	*P*-Value (2-sided)	Mean diff (95% CI)
IgG Pfizer	52.12	29.012	6.49	<**0.0001**	**M1 vs. M5:** −23.10 (−26.04 to −20.16)
				<**0.0001**	**M1 vs. M9** −45.63 (−47.56 to −43.69)
				<**0.0001**	**M5 vs. M9** −22.53 (−24.71 to −20.34)
IgG AstraZeneca	35.32	14.46	2.06	<**0.0001**	**M1 vs. M5:** −20.86 (−23.81 to −17.91)
				<**0.0001**	**M1 vs. M9** −33.26 (−36.75 to −29.76)
				<**0.0001**	**M5 vs. M9** −12.40 (−14.01 to −10.78)
IgG Sinopharm	9.58	3.09	0.00	<**0.0001**	**M1 vs. M5:** −6.49 (−7.86 to −5.12)
				<**0.0001**	**M1 vs. M9** −9.58 (−11.38 to −7.79)
				<**0.0001**	**M5 vs. M9** −3.09 (−3.80 to −2.38)

Bonferroni correction was performed for statistical analyses.

The majority of those events were mild or moderate in severity. Most of the time, people had fever, pain at the injection site, and other systemic problems like fatigue, headaches, and myalgia.[24,25] Also, 13 participants reported experiencing uncommon adverse reactions. As we did not investigate the specific cause behind each adverse reaction, it remains uncertain whether they were directly attributable to the COVID-19 vaccine or if there were other contributing factors. Therefore, 1 of the recommendations is to conduct a follow-up study in the future to explore these uncommon adverse reactions more comprehensively. The limitations of this study were 2-fold. First, the small sample size indicates that the study was conducted with a relatively limited

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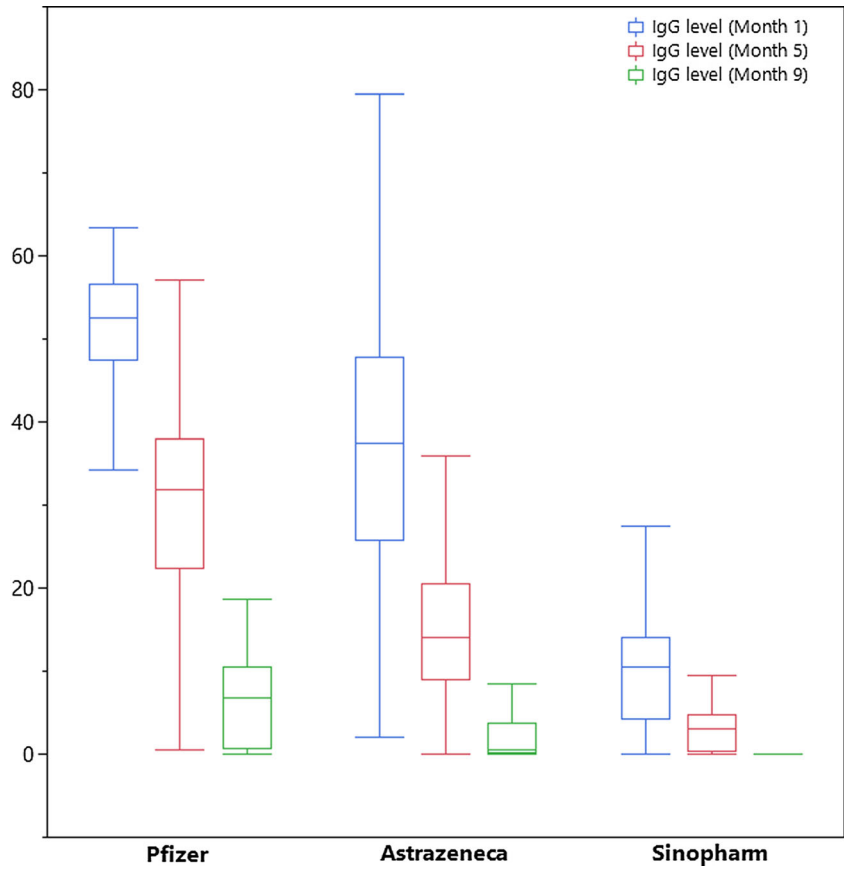

Figure 1. Level of positivity of SARS-CoV-2 anti-spike RBD IgG antibody over 9 mo after the second dose of COVID-19 vaccine.

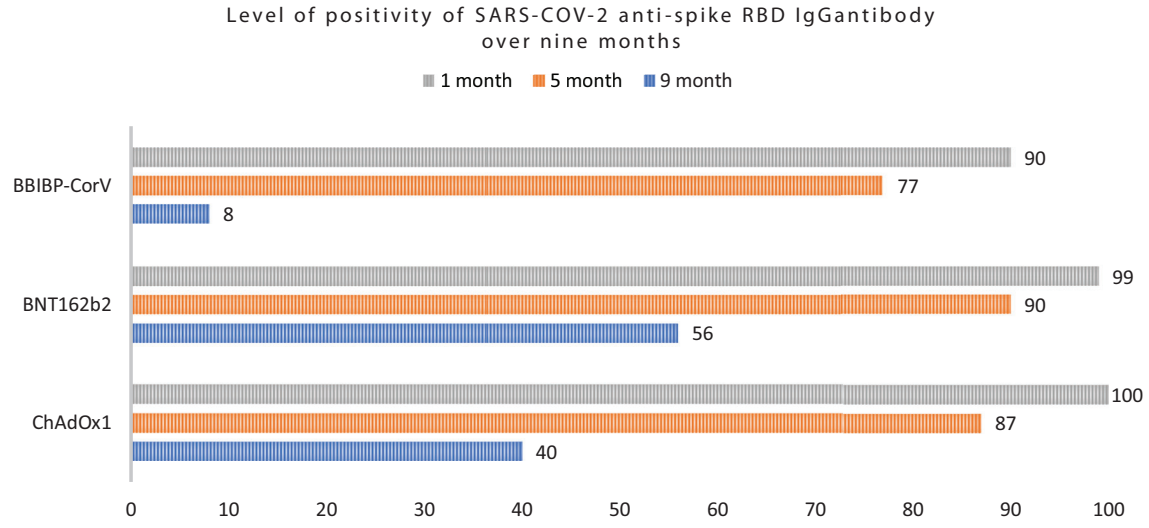

Figure 2. Mean of SARS-CoV-2 anti-spike RBD IgG antibody among health staff after 1, 5, and 9 mo from the second dose of COVID-19 vaccines.

number of participants. This can be a limitation because findings drawn from a small sample may not be representative of the larger population. Second, the study experienced participant dropout during the second and third follow-up periods. Losing cases during the course of a study can impact the study's statistical power. The reasons for the loss of cases were diverse, with some participants leaving the countries and others receiving booster doses.

Conclusions

This study showed that all types of the vaccine (eg, Pfizer BioNTech [BNT162b2], Oxford/AstraZeneca [ChAdOx1], and Sinopharm [BBIBP-CorV]) increase the SARS-CoV-2 anti-spike RBsD IgG antibody. However, the receiver of the Pfizer vaccine has higher SARS-CoV-2 anti-spike RBsD IgG antibodies when examined against time after 1, 5, and 9 mo. Several adverse

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Table 5. Mean of SARS-CoV-2 anti-spike RBD IgG antibody among health staff after 1, 5, and 9 mo from the second dose of COVID-19 vaccines

Level	Mean	SD	*P*-Value	Pairwise mean diff; *P*-value
IgG antibody after 1 mo from the second dose of CIVD-19 vaccine				
Age groups (y)			0.0084	20-30 vs. 41-50 (12.14) P=0.0052
20-30	40.68	16.70		
31-40	33.42	20.89		
41-50	28.53	20.35		
51-60	34.05	21.60		
>60	22.99	13.57		
Female	33.52	21.90	0.7395	NA
Male	34.29	18.30		
IgG antibody after 5 mo from the second dose of CIVD-19 vaccine				
20-30	24.50	13.95	<.0001	20-30 vs. >60 (16.75); P=0.0339
31-40	12.53	10.43		20-30 vs. 31-40 (11.97) P= <.0001
41-50	14.40	13.31		51-60 vs. 31-40 (10.20) P= 0.0026
51-60	22.73	16.71		20-30 vs. 41-50 (10.09) P= 0.0001
>60	7.76	6.062		51-60 vs. 41-50 (8.32) P= 0.0498
Female	17.31	1.14	0.3948	NA
Male	15.91	1.18		
IgG antibody after 9 mo from the second dose of CIVD-19 vaccine				
20-30	4.82	4.59	<.0001	51-60 vs. 41-50 (0.90) P= <.0001
31-40	0.22	0.26		51-60 vs. 31-40 (0.78) P=<.0001
41-50	0.22	0.26		51-60 vs. >60 (1.61) P= 0.0029
51-60	6.6	6.66		20-30 vs. 41-50 (0.73) P=<.0001
>60	0.68	1.02		20-30 vs.31-40 (0.56) P=<.0001
Female	2.40	3.45	<.0001	NA
Male	0.25	0.26		

Table 6. Distribution of participants according to an adverse reaction by type of COVID-19 vaccines from 12 h to 1 mo after the first and second dose of vaccines

	First dose			Second dose		
Common adverse reactions	ChAdOx1	BNT162b2	BBIBP-CorV	ChAdOx1	BNT162b2	BBIBP-CorV
Tiny red spot on the skin	1	0	0	0	1	0
Shortness of breath	3	2	0	0	2	0
Nausea and vomiting	8	1	0	0	2	0
Stomach pain	10	12	2	8	14	0
Chills	17	7	2	6	11	2
Fatigue	18	9	11	0	0	0
Swollen lymph node	19	39	7	0	2	0
Shoulder pain	22	12	21	22	12	21
Headache	32	21	13	20	34	12
Joint pain	37	21	17	12	40	2
Muscle pain	39	27	25	21	35	16
Fever	58	43	23	19	39	7

reactions have been observed and commonly reported across the globe, including chills, muscle and joint pain, headache, fever, and pain at the site of injection. This study, however, found uncommon adverse reactions such as increased appetites and better sex activity among Pfizer vaccinees. In comparison, loss of appetite and lower sex activity were reported among respondents who got Sinopharm vaccines. While the uncommon adverse reaction was found among a very small percentage of the participants, it is worth noting for future investigation.

The implication of this study could be summarized in 3 points: first, higher and potentially longer antibody responses can be obtained if the mRNA vaccine (such as BNT162b2) is given as compared to other vaccines. This result means that authorities should consider this factor when requesting the vaccine. Second, the booster doses of the COVID-19 vaccine are highly recommended because more than 50% of the participants either have become anti-spike protein negative or have a deficient level of anti-spike protein against COVD-19 vaccines. Third and last,

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Table 7. Distribution of uncommon adverse reactions by type of COVID-19 vaccines during 12 h to 1 mo

Uncommon adverse reaction	ChAdOx1	BNT162b2	BBIBP-CorV
Period irregular	2	1	0
Hypertension	5	1	2
Loss of appetites	0	0	1
Increase appetites	3	6	0
Pain limb and neck	0	3	0
Sex activity is better as compared to before the vaccine	0	4	0
Sex activity is less as compared to before the vaccine	0	0	5
After 5 d from the last dose, muscle pain, back pain, and took treatment	0	1	0
Back pain	0	2	0
Cannot wear mask after vaccines and I feel short breathing	0	1	0
Depression for 2 mo after vaccine	1	0	0
Diarrhea for 2 d	2	0	0
Herpes after first dose	0	1	2
No adverse effect	87	80	90
Total	100	100	100

which is related to the uncommon adverse reaction that should be further investigated.

Data Availability Statement. The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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Competing interests. The authors declare no conflict of interest for this study.

Ethical standards. Ethical approval was obtained from the General Directorate of Health in Duhok under number (06052021-4-4) dated June 14, 2022. Informed consent was obtained from all participants who were willing to participate in the investigation before any procedure was performed as part of the investigation by a trained member of the investigation team. Each participant has been informed that participation in the investigation is voluntary and that s/he is free to withdraw, without justification, from the investigation without consequences and without affecting professional responsibilities.

Institutional Review Board Statement. The study was conducted according to the guidelines of the Ethics Committee of Duhok Health directorate and Duhok Polytechnic university (Approval number: (06052021-4-4) dated June 14, 2022).

Informed Consent Statement. Informed consent was obtained from all subjects involved in the study.

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