Research Article

Variety of Antibody Responses to BNT162b2 and BBIBP-CorV Vaccinations Against COVID-19 Infections in Baghdad and Fallujah, Iraq

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Abstract

The huge impact of COVID-19 worldwide led to the rapid development of vaccines with inadequate data about its longevity, effectivity, and safety. This study aims to evaluate the effectiveness and safety of COVID-19 vaccines available in Iraq and to measure longevity of created antibody response among different time points of both Pfizer-BioNTech and Sinopharm vaccines in Baghdad and Fallujah, Iraq.

A two-axis method was used: the first was cross sectional study on the vaccination state for COVID-19 in Baghdad and Fallujah, using an online survey contained questions about city, vaccine type, side effect, pre and post infections, and chronic diseases. The second part involved a prospective observational study of the vaccine's immunological effectiveness and stability in 60 serum samples from completely vaccinated individuals (second dose) of Pfizer or Sinopharm along different time points (1 - 6 months) by measuring the SARS-CoV-2 Anti-RBD-IgG concentration and evaluating its correlation with pre-infection with COVID-19.

Among different types of vaccines available in Iraq, people in Baghdad and Fallujah preferred Pfizer vaccine over other available types, particularly those with chronic diseases. No statistically significant difference was noticed between IgG concentrations at different points of time, IgG concentrations in Pfizer vaccinated individuals were more elevated than Sinopharm, and all of Pfizer vaccinated people showed positive results. Our study established a synergistic impact between recent COVID-19 infection and vaccination, leading to increased levels of IgG antibodies, notably in individuals who received the Pfizer vaccine. Additionally, our findings demonstrate that IgG concentrations remained stable in vaccinated individuals even six months after completing the vaccination with second dose.

Keywords: Antibody Responses, BNT162b2, BBIBP-CorV, COVID-19, IgG.

1. Introduction

The huge impact that COVID-19 had worldwide, increase morbidity and mortality, paralysing world economics, in addition to the psychological consequences on individuals and communities (Tsang et al., 2021) as the vaccine

development process had to be fast and accurate. The current advance in molecular biology and genetics and the fact that almost all structural and functional components of SARS-CoV-2 have been deciphered, paved the way towards the development of several vaccine types (Marian, 2021). Urgency for vaccine development, along with the need to surpass certain trial requirements, placed immense pressure on researchers to conduct a thorough study of the vaccine's safety and efficacy. This was crucial in order to alleviate doubts or reservations among the general public (Lazarus, 2021). The need to promote vaccine uptake and prevent its transmission from COVID-19 infected individuals to others, including ineligible friends and family members and individuals at higher risk of severe illness, has prompted the need for a study on the efficacy of vaccines in Iraq particularly Baghdad and Fallujah cities, preference of vaccine type among male and female individuals, and the safety of vaccination for individuals with chronic illnesses.

Several published reports and studies have documented various side effects and efficacy outcomes associated with the administration of vaccines. Many of these studies have focused on investigating the duration of immunity conferred by the vaccine, as well as the interplay between vaccination and infection in modulating individual immune responses. Such investigations aim to elucidate the factors underlying differences in vaccine efficacy and immunity with the ultimate goal of optimizing vaccine strategies to enhance protective immunity (Almufty et al, 202; Bulut & Kato, 2020).

The study aimed to evaluate the effectiveness and safety of COVID-19 vaccines available, namely Pfizer's 'BNT162b2', Sinopharm's 'BBIBP-CorV', and Oxford-AstraZeneca's 'ChAdOx1', in some areas of Iraq. For the rest of the paper, the vaccine types will be referred to by their company names for simplicity. In addition, our study aimed to report the vaccine with the highest side-effects, the effect of recent infection or post-infection on side-effect, to measure the SARS-CoV-2 Anti-RBD-IgG concentration in different time points after periods of 1, 2, 3, 4, 5, and 6 months of vaccination to estimate the duration of antibody lasting and the decrease in antibody titer over time. Furthermore, we investigated the relationship between recent infection (one that has occurred more than two- three weeks prior to vaccination) (Centers for Disease Control and Prevention, 2021) and the type of vaccine and individual's age and gender in response to the time points.

2. Material and Methods

The first part of the study is a survey on the vaccination state of COVID-19 vaccines in Baghdad and Fallujah, which was conducted on 498 participants. The questionnaire was distributed from 20 August 2021 using an online survey platform to 20 November 2021. The following information was collected in the questionnaire: gender, age, address, having any chronic diseases, an infection of COVID-19 before vaccination, type of vaccine (restricted to the types used in Iraq: Pfizer, Sinopharm, and Oxford-AstraZeneca), number of doses, side-effects following vaccination, and infection with COVID-19 after vaccination.

The second part of the study was carried out at the laboratories of the College of Applied Sciences, University of Fallujah in Falluja, Iraq with the aim of quantifying IgG antibody concentrations in randomly selected samples of forty-six blood specimens. The specimens were obtained from individuals residing in Fallujah city who had been fully vaccinated two doses with either Pfizer or Sinopharm vaccines between the 30 of December 2021 and 26 of January 2022. The study participants were asked to provide information about their age, gender, vaccination status including type of vaccine received, and time elapsed since completion of the second dose ranging from 1 to 6 months for each vaccine type. In addition, any prior COVID-19 infections were assessed to exclude any confounding effects of infection-induced antibodies on the measured vaccine-induced antibodies. Notably, none of the selected blood specimens exhibited evidence of SARS-Cov2 infection after vaccination.

Venipuncture was used to collect blood samples drawn into gel tubes containing a clotting activator. The samples were then centrifuged at 1210 xg for 10 minutes (BOECO, Germany). The supernatant was transferred to plain tubes and stored at -18° C until further use.

2.1. Determination of IgG Concentration Using MINI-VIDAS Immune Analyser

Serum samples were used after warming to room temperature, then using VIDAS® SARS-COV-2 IgG (BIOMÉRIEUX, France) kit, SARS-COV-2 IgG test was performed by MINI-VIDAS immune analyser (BIOMÉRIEUX, France). Results were interpreted as follows:

$i < 1.00$	Negative	IgG antibodies to SARS-CoV-2 (not detected)
$i \geq 1.00$	Positive	IgG antibodies to SARS-CoV-2 (detected)

2.2. Statistical Analysis

The Statistical Analysis System- SAS (2012) and SPSS v.26 programs was used to conduct a Chi-square test to compare percentage under probability (0.05 and 0.01).

3. Results

The t study surveyed a sample of 498 individuals who had been vaccinated with one of three available vaccines against COVID-19, namely (Pfizer's 'BNT162b2', Sinopharm's 'BBIBP-CorV', and Oxford-AstraZeneca's 'ChAdOx1'). Our results indicate that the Pfizer vaccine was significantly preferred by residents of Baghdad and Fallujah as demonstrated in Table (1).

Moreover, the data collected from the study group, which represents a subset of the Iraqi population, revealed significant age-related differences ($p<0.01$) in vaccination uptake regardless of the vaccine type. The highest number of vaccinated individuals (377) belonged to the young adults (20-29 years old), the majority of which received the Pfizer vaccine (see Table 1).

Table 1. The distribution of vaccinated individuals with different types of vaccines according to their ages and gender state.

Type of vaccine/Age groups	Pfizer		Oxford- Astrazeneca		Sinopharm		Total
	Male	Female	Male	Female	Male	Female	
<20 year	12	27	3	4	4	8	**58**
20-29 year	81	223	7	12	23	31	**377**
30-39 year	12	10	24	15	24	21	**106**
40-49 year	15	5	9	9	32	8	**78**
>50 year	21	18	12	13	20	9	**93**
Total	**141**	**283**	**55**	**53**	**103**	**77**	**498**

Our results also revealed that among the vaccinated individuals, those who received the Pfizer vaccine experienced significantly higher incidence of side effects, with fever being the most predominant (220 cases), followed by fatigue and pain at the injection site, as shown in Table (2).

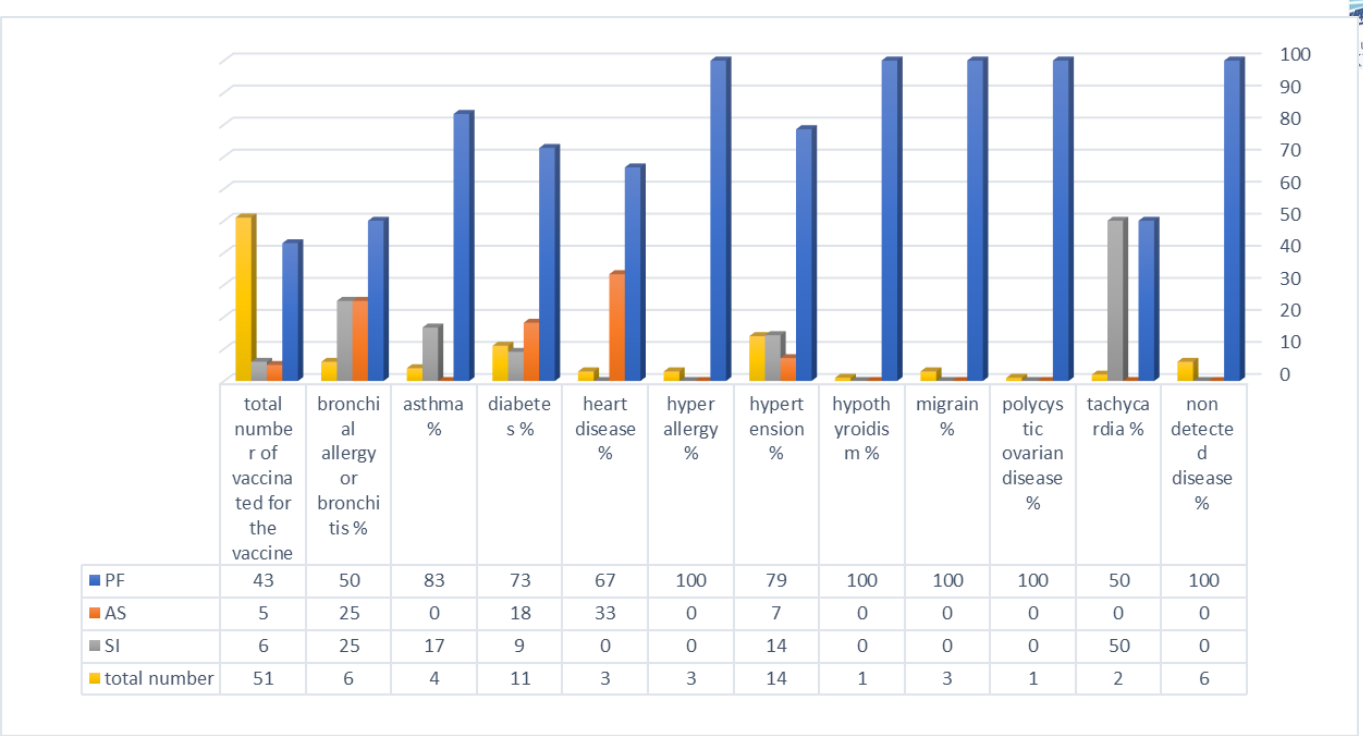
Table 2. Number of vaccinated individuals with three types of vaccines classified based on having specific types of side effects after first and second doses of vaccination.

Type of Vaccine	Fever	Fatigue	Nausea	Headache	Pain At Injection Site	Muscle Pain	Lymph Enlargement	Tachycardia
PF	82%	82%	88%	89%	88%	83%	100%	100%
AS	8%	7%	0 %	5%	6%	6%	0%	0%
SI	10%	10%	13 %	6%	6%	11%	0%	0%
Total	**220**	**164**	**8**	**79**	**140**	**36**	**3**	**3**

Out of the total 498 vaccinated individuals, 51 were identified as having recent chronic diseases, and these cases were distributed as shown in Figure (1).

The analysis revealed significant differences in vaccine preference among individuals with chronic diseases, with the Pfizer vaccine being the most commonly chosen option. In addition, no significant correlation between recent COVID-19 infection and the incidence of contraindications after vaccination. Moreover, the vaccination does not seem to prevent infections with COVID-19 later; neither after partial (first dose) nor complete vaccination (second dose), as shown in Table (3).

The second part of our study investigates the difference in IgG concentrations between two types of COVID-19 vaccines, Pfizer and Sinopharm over different periods, and the results demonstrated significant difference ($P=0.034$). The study included individuals with a mean age of 23.5 years and no significant correlation between IgG concentrations and gender was found.



	total number of vaccinated for the vaccine	bronchial allergy or bronchitis %	asthma %	diabetes %	heart disease %	hyper allergy %	hypertension %	hypothyroidism %	migrain %	polycystic ovarian disease %	tachycardia %	non detected disease %
PF	43	50	83	73	67	100	79	100	100	100	50	100
AS	5	25	0	18	33	0	7	0	0	0	0	0
SI	6	25	17	9	0	0	14	0	0	0	50	0
total number	51	6	4	11	3	3	14	1	3	1	2	6

Figure 1. Percentage of patients vaccinated with specific vaccine relevant to the presence of chronic disease.

Table 3. Distribution of (Pfizer and Sinopharm vaccines) vaccinated individuals, based on their recent infection and post-infection status.

Type of vaccine	Recent infection	Post-infection	Total patient vaccinated
PF	82%	84%	402
AS	4%	16%	30
SI	13%	0%	66
Total	**210**	**25**	**498**

The results indicated a significant difference in IgG concentrations between the two vaccine types studied with Pfizer-vaccinated individuals exhibiting higher concentrations than Sinopharm-vaccinated individuals. In the first few months after vaccination, the IgG concentration results for the Pfizer group were convergent but lower than the initial period, with no significant differences between those periods. In contrast, the highest concentration of IgG in the Sinopharm group was observed six months after vaccination (20.1950 ± 18.91924) as shown in Table (5).

The difference in IgG concentrations between individuals with recent COVID-19 infection and those with no recent infection have been examined and the results show that those with recent infection had higher IgG concentrations (21.3880±15.89587) than those without, but the difference was not statistically significant. This indicates that the production of IgG as a response to infection did not significantly affect the IgG concentration resulting from vaccination as demonstrated in Table (4).

Table 4. IgG concentration distribution means based on the onset of recent infections with two types of vaccine (BNT162b2 and BBIBP-CorV).

Infection	Mean	SD	No.
NO	19.6943	15.47323	35
YES	21.3880	15.89587	11

able 5. IgG concentration of individuals with different types of vaccine (Pfizer 'BNT162b2' and Sinopharm 'BBIBP-CorV') according to the period of vaccination and gender.

Period after vaccination	Type of vaccine	Gender	Mean	SD	No. of samples
1M*	PF	F	39.4025	6.08782	4

		M	0	0	0
		Total	39.4025	6.08782	4
	SI	F	2.1700	-	1
		M	0	0	0
		Total	2.1700	-	1
	Total	F	31.9560	17.46562	5
		M	0	0	0
		Total	31.9560	17.46562	5
2M	PF	F	36.2500	6.59024	2
		M	35.7067	10.39968	3
		Total	35.9240	8.06369	5
	SI	F	2.4800	-	1
		M	0	0	0
		Total	2.4800	-	1
	Total	F	24.9933	20.04628	3
		M	35.7067	10.39968	3
		Total	30.3500	15.44135	6
3M	PF	F	28.2300	9.77222	2
		M	36.7933	3.37000	3
		Total	33.3680	7.17995	5
	SI	F	25.4200	-	1
		M	4.0050	.00707	2
		Total	11.1433	12.36396	3
	Total	F	27.2933	7.09790	3
		M	23.6780	18.11632	5
		Total	25.0338	14.33314	8
4M	PF	F	22.7467	14.07661	3
		M	18.6900	-	1
		Total	21.7325	11.67111	4
	SI	F	3.9533	2.26144	3
		M	.2700	-	1
		Total	3.0325	2.60790	4
	Total	F	13.3500	13.68440	6
		M	9.4800	13.02491	2
		Total	12.3825	12.69661	8
5M	PF	F	14.5650	8.54892	2
		M	30.2133	6.64894	3
		Total	23.9540	10.66941	5
	SI	F	0.4500	0.22650	3
		M	0.4900	0.53740	2
		Total	0.4660	0.31358	5
	Total	F	6.0960	8.83553	5
		M	18.3240	16.94755	5
		Total	12.2100	14.27879	10
6M	PF	F	22.5725	9.81420	4
		M	10.7700	-	1
		Total	20.2120	10.00493	5
	SI	F	20.2150	19.77778	2
		M	20.1750	26.12760	2
		Total	20.1950	18.91924	4
	Total	F	21.7867	11.72626	6
		M	17.0400	19.25644	3

		Total	20.2044	13.57483	9
Total	PF	F	27.8959	11.79563	17
		M	30.6909	10.27705	11
		Total	28.9939	11.11313	28
	SI	F	7.6100	11.34143	11
		M	7.0871	14.01215	7
		Total	7.4067	12.04279	18
	Total	F	19.9264	15.22768	28
		M	21.5117	16.48088	18
		Total	20.5467	15.56769	46

* A significant difference (p value=0.03) between IgG concentrations in types of vaccines along different time points.

4. Discussion

With the emergence of new variants of the SARS-CoV-2 virus, the importance of minimizing the negative effects it had on the human communities became crucial to restore normal life routine. Many vaccines have been developed, and it became necessary to study their side effects and effectiveness in minimizing the risk of disease. Such studies may aid addressing some mis-informed persons and to dispel any misinformation surrounding them.

The result suggests that, out of the Pfizer, Sinopharm and AstraZeneca vaccine types available in Iraq, Pfizer vaccine is the most acceptable and chosen vaccine in Baghdad and Fallujah cities. The preference of the Pfizer vaccine is likely to be due to its reputation based on the report published by the Centers for Disease Control and Prevention (2022).

There appears to be gender difference in the willingness to take different COVID-19 vaccines in our study, with females showing greater reluctance towards receiving the AstraZeneca and Sinopharm vaccines, with 53 and 77 vaccinated female individuals, respectively, compared to a total of 283 female individuals vaccinated with the Pfizer vaccine. This may be attributed to published reports indicating a higher incidence of adverse effects in females vaccinated with AstraZeneca, including life-threatening clotting issues (Urakawa, 2022). This finding is consistent with the results reported by Almufty (2021) stating that "*female gender was at significant risk factor for adverse effects (P value 0.028) where younger individuals and females tend to develop stronger immune responses than older individuals and males*".

Of the 332 women included in the study, 259 experienced a range of significant side effects, which may be explained by many factors; some are related to the general female immune response to vaccines (Demonbreun, 2021), and some are related to SARS-CoV-2 vaccines exclusively (Fischinger et al., 2019).

According to Ricotta, 2022, COVID-19 poses a threat to chronic disease patients. Therefore, the tendency of chronic disease patients toward the Pfizer vaccine more significantly, can be attributed to several factors that influence their choice of vaccine type. These factors include the lack of sufficient information regarding the safety of vaccines for individuals with chronic diseases, the guidance provided by Iraqi government healthcare authorities, and the recommendations from the World Health Organization (WHO) encouraging these patients to receive vaccination in order to mitigate the heightened risk of contracting the infection. (World Health Organization, 2022) All of these factors may cause such patients to choose the 'safest' vaccine type based on available information. According to the report of WHO, 2021 the AstraZeneca vaccine was mainly administered to individuals aged 50 years and older, most of which had comorbidities.

In a study by Almufty, 2021 both ages of participant (less than 50 years old) and gender factors affected AstraZeneca vaccinated individuals, particularly those with comorbid disease such as hypertension, diabetes, asthma, etc., who represent the most susceptible people to develop symptoms after vaccination, especially in females. Other studies suggested that COVID-19 infections in type 1 diabetic's patient for example, may be more fatal (Grzelakowska, 2021 & Gurbel, 2021).

According to the published information by (CDC, 2022), the most commonly reported systemic side-effects were fever, fatigue and headache, which agrees with the findings of Almufty et al. (2021), which were significantly higher in AstraZeneca followed by Pfizer and Sinopharm vaccines.

The largest number of adverse effects obtained in this study was from the Pfizer vaccine. While most of these effects were mild contraindications, the higher number may be attributed to the fact that the largest number of individuals in the study were vaccinated with the Pfizer vaccine. However, it has been stated that three cases of tachycardia reported in individuals who received the Pfizer vaccine, which were not related to the presence of pre-existing chronic tachycardia prior to vaccination.

According to a study by Kang (2021) the presence of intense local or systemic reactions after a second dose of BNT162b2 vaccine can be attributed to the mRNA vaccines structure, and lipid nanoparticle (LNP) delivery agents, such as LNPs and polyethylene glycol. It is important to note that adverse events, while associated with stronger immune responses may have implications for antibody production. Subsequently, the occurrence of fewer adverse events could potentially lead to reduced levels of antibody production (Mitchell & Casella, 2017).

The humoral antibody response (measured by IgG titers) was evaluated following vaccination with Pfizer and Sinopharm vaccines. AstraZeneca was excluded from the study due to the small number of individuals been vaccinated with it at the time (Buonfrate et al., 2021; Polack et al., 2020). The persistence of antibody levels up to 6 months after the second dose of the vaccine (ranging from 1 to 6 months) have been assessed. Sinopharm produced lower IgG concentration with a number of seronegative patients compared to Pfizer, representing a lower effectiveness of this vaccine (Ferenci & sarkadi, 2022).

A drawback that was encountered in the study was that IgG in the period (1-6 months) for the same patient were not assessed. This was caused by the length of time required for watching and measuring IgG and the difficulty of monitoring the patients for this extended period. The study results indicated higher IgG concentrations in Pfizer-vaccinated than Sinopharm-vaccinated individuals as shown in Table (5). Additionally, it is noteworthy that a significant proportion of vaccinated individuals in this study were either asymptomatic or experienced minimal symptoms. As a result, their antibody production levels may be comparatively lower (Demonbreun et al., 2021).

All participants in the study vaccinated for Pfizer were seropositive for IgG. The mean concentration of IgG after one month of vaccination with Pfizer was 39.4025±6.08782 IU/mL which is higher than the results obtained by Heyming (2021) where 98.4% tested positive for IgG and the average was 22.1 after 17–36 days of patients that received BNT162b2.

The presence of mild to more severe symptoms during past SARS-CoV-2 infection has been shown to enhance antibody response after vaccination (Buonfrate et al., 2021). The efficacy of the BNT162b2 vaccines against symptomatic laboratory-confirmed SARS-CoV-2 infection has been reported in a large randomized controlled clinical trial as 95% after the second dose of the vaccine (Walsh et al., 2020; Polack et al., 2020).

The potential correlation between age and the level of immune response (IgG concentration) have not been investigated due to the distribution of data that have been collected. The average age of the study's participants was 23.5 years which may indicate the presence of good antibody response in Pfizer vaccinated individuals. Additionally, as the immune system tends to weaken with age, it may result in a less robust immune response to vaccines in older individuals compared to younger ones. Moreover, it has been observed that women generally mount stronger immune response than men, which may also contribute to differences in vaccine response between genders (Fischinger et al, 2019).

The study states a decline in the overall antibody titre observed with increasing age in the case of Sinopharm vaccine. Additionally, a significant proportion of elderly individuals (>50 years) vaccinated with Sinopharm vaccine had undetectable antibody levels.

The results show that Pfizer vaccine is the most, and Sinopharm and AstraZeneca vaccines are the least, vaccines used in Baghdad and Fallujah cities of Iraq amongst the populations that have been examined. The highest age group recipient of vaccines was 20-29 years. IgG concentrations after vaccination with Pfizer vaccine was significantly higher than Sinopharm vaccine. There were no significant differences in IgG concentrations observed between different time points up to six months after complete vaccination (two doses). Additionally, recent infection did not appear to have an effect on IgG concentration after a two-dose vaccination.

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