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Research Article

Differences in IgG and IFN γ levels generated against different types of vaccines available in Iraq.

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ABSTRACT

Objective: The SARS-CoV2 vaccines are the most effective and promising way to fight this widespread viral pandemic, but there is little information about which vaccines are better for various populations, particularly among Iraqi people living in Karbala Province. Thus, the aim of the current study is to investigate the differences in IgG and IFN γ concentrations generated against three types of vaccines available in Iraq.

Method: Cross-sectional study was conducted between November 2021 and April 2022. A blood sample was obtained from 174 vaccinated persons. SARS-CoV-2 IgG levels were detected using SARS-COV-2 IgG II quant assay on the ARCHITECT I system and interferon gamma level detection was performed utilizing human IFN- (interferon).

Result: Out of 174 vaccinated persons. Ninety subjects were men and 84 were women with ages ranging from 18 to 70 years. AstraZeneca and Sinopharm's vaccines had lower IgG and IFN γ concentrations as compared to Pfizer's vaccine. Significant differences among the three types of vaccine within both age groups was observed. The mean IgG concentration was higher in males than females in subjects vaccinated with Pfizer and AstraZeneca. No significant differences in IFN-γ according to age. The mean level of IFN γ in females were higher than that in males in subjects vaccinated with Pfizer and Sinopharm.

Conclusion: Participants vaccinated with Pfizer vaccine produces the highest antibody concentration and IFN γ as compared to AstraZeneca and Sinopharm vaccines. younger participants under the age of 25 had higher antibody and IFN γ concentrations than older participants vaccinated with Pfizer and Sinopharm but not for the significant level. Regarding Sex, Pfizer vaccine produce higher antibody level and less IFN γ in males than females whereas Sinopharm vaccine produce higher antibody and IFN γ levels in females.

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Introduction:

SARS-CoV-2 is the primary cause of most COVID-19 infections worldwide (CDC, 2020) , it was a new and unique coronavirus strain that caused respiratory and gastrointestinal infections in humans for the first time (Pal et al., 2020). The virus was rapidly spreading from its origins in Wuhan City, China, to the rest of the world(Liu et al., 2020). Globally, there were approximately 554 million COVID-19 cases and 6.35 million fatalities as of July 7, 2022, in Iraq 2.44 M cases and 25,311 deaths (WHO, 2020) . The majority of virus-infected people will suffer from a mild to severe respiratory illness and will recover without the need for special treatment(Papa et al., 2020). It can spread by either direct or indirect contact with infectious respiratory droplets or fomites on mucous membranes (such as the eyes, nose, or mouth). Risks of transmission rise with time and proximity to contacts/infected people (Schilling-Loeffler et al., 2022).

Within the coronavirus particle A nucleoprotein (N) wraps the RNA genome to create a coiled tubular structure, this helical nucleocapsid was encased in the viral envelope (E). With the viral envelope are two or three structural proteins. The envelope contains the matrix protein (M). The target of the neutralizing antibody was the spike structural protein (S) anchored in the envelope (Thomas, 2020) (Gupta et al., 2021). It's crucial to develop protection against the SARS-CoV-2 coronavirus to control the COVID-19 pandemic, protect people from serious illness, and stop the viral transmission (WHO,2021). In response to an infection or a vaccination, the immune systems defend the body against SARS-CoV-2 (Chang & Radbruch, 2021). Two distinct types of immunity will be generated in response to infection or vaccination. One is cell-mediated, or T-cell- and other is mediated by antibodies (Chaplin, 2010).

Vaccinations can be classified as either classical or new generation according to the most often used classification scheme (Simões & Rodríguez-Lázaro, 2022). In contrast to new vaccines, which use nucleic acids, viral vectors, or antigen-presenting cells, classical vaccinations use live, inactivated, or virus-like particles and protein components (Abu-Halaweh et al., 2021). The first and most common vaccine enters in Iraq in 2 march 2021 were Inactivated SARS-CoV-2 vaccine developed by Sinopharm a state-owned Chinese company, it's taken intramuscularly as two doses (0.5 mL) with efficacy reach to 79% (Zahid et al., 2021). The Astra Zeneca vaccine it's a British - Swedish multinational pharmaceutical and biotechnology company, it have embraced a recombinant vaccine by engineering a chimpanzee adenovirus to carry DNA for the spike antigen where enter to Iraq in 25 March 2021. WHO recommended giving it intramuscularly (0.5 mL) in two doses with an interval of eight to twelve weeks with efficacy 72% (Ramasamy et al., 2020). Then after, Pfizer (BioNTech) adapted nucleoside modified mRNA for the vaccine, Pfizer is a global pharmaceutical manufacturing company headquartered in New York City, New York State, USA. It is an American multinational pharmaceutical company its protection begins to develop twelve days after the first dose, but full protection needs 2 doses and it enter to Iraq in 1 December 2021. World Health Organization recommends to be administered with a 21-to-28-day interval with efficacy reach to 95% (Walsh et al., 2020). Despite the impressive data on the COVID 19 vaccine that has been published, there is still a lack of knowledge regarding the kind of vaccination techniques that will be most effective in a given community (Garcia-Beltran et al., 2021). Individual humoral and cellular responses to the S protein are extremely diverse, and quantitative measuring of IgG (as a marker for humoral immune response) and IFN γ (a marker for cellular immune response) produced after vaccination in many individuals who have undergone a variety of vaccines might possibly provide essential data for updating vaccine development.

Thus, the aim of this research is to evaluate the humoral and cellular immune response among subjects' vaccination with different types of vaccines in respect to some risk

factors such as age, sex, previous infection and doses.

Method

From November 2021 to April 2022, a cross-sectional study of people who had received the COVID-19 vaccination was conducted in the College of Applied Medical Sciences at the University of Kerbala. Participants were from both sexes. The information for each participant was documented according to the questionnaire form, which include age, sex, type of vaccine taken, dose and other information. Five milliliters of blood were collected. The SARS-CoV-2 IgG II Quant antibody test, which uses chemiluminescent microparticle immunoassay (CMIA) by Abbott (Germany) device for the qualitative and quantitative measurement of IgG antibodies to SARS-COV-2 in human serum, was used to identify SARS-CoV-2 IgG levels. Interferon gamma level was measured using Human IFN-γ (Interferon Gamma) ELISA Kit according to procedure mentioned by sunlong (China). Device used was full automated ELISA Human (Germany) and the unit of measurement was Pg/ml .

Statistical analysis

IBM SPSS VERSION 24 software was used for statistical analysis of data. Quantitative results are indicated as mean ± SD. Pearson test was used for analyzing correlations between parameters. The statistical significance level was set at $P<0.05$. ANOVA table to compare three vaccine and independent sample t test to compere groups and LSD to test less significant deference

Results

Serum Blood samples was collected from One hundred and seventy-four patients, between 1 November 2021 to April 2022 in Karbala, Iraq. The collected blood was drown in to gel tube, centrifuged at 2000 rpm for 20 min, and then serum was separated and kept in deep freeze. The majority of participant were medical student in Kerbala university. The participants' ages are ranged from 18 to 70 years, the mean age was 25.97, they were divided into 2 groups: those under 25 years old (62.6%), and those over 25 years old (37.3%). Ninety subjects (51.7%) were men and eighty-four (48.2%) were women. One hundred and five out of 174 (60.3%) had received the Pfizer vaccine, fifty-nine (33.9%) had received the Sinopharm vaccine, and ten (5.7%) of them had received AstraZeneca. The sample was taken at various times and weeks after vaccination. Some of them had received one dose (39.6%) while the others had received two doses (60.3%), as shown in Table (1).

Table (1) Demographic Data of the participants

Variables		Frequencies (%)
Gender	Female	84 (48.2%)
	Male	90 (51.7%)
Age (Mean ±SD 25.97 9±.327)	More than 25	65 (37.3%)
	Less than 25	109 (62.6%)
Dose	First	69 (39.6%)
	Second	105 (60.3%)
Type of vaccine	Pfizer	105 (60.3%)
	Sinopharm	59 (33.9%)
	AstraZeneca	10 (5.7%)

Comparison of IgG and IFN-γ concentration generated against the three types of vaccines

Comparing anti-spike (IgG) levels among the three types of vaccines revealed significant difference. AstraZeneca and Sinopharm's vaccines had lower IgG concentrations as compared to Pfizer's vaccine. and comparison of IFN γ levels among the three types of vaccines revealed no significant difference, as shown in Table (2).

Table 2 Comparison of IgG and IFN γ level generated against the three types of vaccines

Type of vaccine	IgG AU/ml	IFN-γ pg/ml
	Mean ± S. D	Mean ± S. D
Pfizer	16960.6 ±11092.0	64.6 ±14.7
Sinopharm	4118.3 ±1380.3	64.2 ±12.5
AstraZeneca	3195.6 ±658.6	60.9 ±12.1
P value	0.00	0.719
ISD	2793	

Differences in IgG and IFN γ according to age groups

The overall antibody concentration in participants under the age of 25 was higher than that in people above the age of 25. Also, there were significant differences among the three types of vaccine within both age groups, and the highest concentration was seen in participants vaccinated with Pfizer, as shown in table (3). Despite this, the current study does not observe any significant difference in IgG concentration between persons younger and older than 25 whom vaccinated with Sinopharm and Pfizer vaccines, whereas, there is a significant difference between the two age groups in subjects vaccinated with the AstraZeneca vaccine.

With the exception of the AstraZeneca vaccine, there were no significant differences in IFN γ levels between the two age groups or within either group, as shown in table (3). However, the mean level of IFN γ for the subjects whom less than 25 years were higher than that in subjects with more than 25 years.

Table 3 differences in IgG and IFN-γ according to age group

Type of vaccine	IgG AU/ml			IFN-γ Pg/ml		
	Less than 25	More than 25	P value	Less than 25	More than	P value
	Mean ± S. D	Mean± S. D		Mean± S. D	Mean± S. D	
Pfizer	18329.5±11461.0	14714.2±10204.8	0.109	65.5±14.9	63.1±14.5	0.429
Sinopharm	4110.8±1274.8	4132.5±1597.1	0.955	64.5±13.1	63.8±11.7	0.852
AstraZeneca	3551.1±446.3	2662.4±580.9	0.025	67.0±8.3	51.7±11.5	0.04
Total	12505.6±11301.4	10589.8±9634.8		65.2±13.9	62.6±13.6	
P value	0.00	0.00		0.89	0.252	
LSD	3577	4405				

Differences in IgG and IFN γ levels with Sex

As shown in table (4), the current study revealed that there was significant difference in IgG concentration among the three types of vaccines within male and female subjects and the antibody production was higher in participants vaccinated with Pfizer. The mean of the IgG concentration was higher in males than females in subjects vaccinated with Pfizer and AstraZeneca. However, no significant difference between males and females' subjects was observed for each type of vaccines. Regarding the IFN γ, there were no significant differences neither among the three types of vaccines, nor between males and females for each vaccine despite that the mean level of IFN γ in females were higher than that in males in subjects vaccinated with Pfizer and Sinopharm. The IFN γ level was higher in males in comparison to females in subjects vaccinated AstraZeneca.

Table .خطأ! لا يوجد نص من النمط المعين في المستند. deferent in IgG and IFN-γ level with sex

Type of vaccine	IgG AU/ml			IFN-γ Pg/ml		
	Male	Female	P value	Male	Female	P value
	Mean ± S. D	Mean± S. D		Mean± S. D	Mean± S. D	
Pfizer	17030.8±11011.8	16877.0±11305.4	0.945	62.7±14.5	66.9±14.7	0.155
Sinopharm	3927.1±1001.5	4273.7±1624.5	0.346	62.7±11.6	65.5±13.3	0.413
AstraZeneca	3251.4±546.2	2972.5±1300.4	0.622	63.3±12.3	51.1±3.3	0.216
Total	12020.4±10820.5	11554.6±10687.6	0.95	62.8±13.4	65.9±14.1	
P value	0.00	0.00		0.99	0.70	
LSD	4081	3928				

Differences of IgG and IFN γ concentrations according to dose

As shown in table (5), there was no significant variation between the first and second dose for each type of the three vaccines However, there was a significant difference in IgG concentration between the Pfizer vaccine and Sinopharm for the first dose, and among the three types of vaccine in the second dose. The highest concentration was seen in Pfizer vaccine.

Regarding IFN γ, there were no significant difference between the first and second doses for each type of vaccines and among the first dose and second dose for all types of vaccines.

Table 5. Differences of IgG and IFN γ concentrations according to dose

Type of vaccine	IgG			IFN gamma		
	dose 1	dose 2	P value	dose 1	dose 2	P value
	Mean ± S. D	Mean± S. D		Mean± S. D	Mean± S. D	
Pfizer	18123±11062	15905±11116	0.313	66±13	64±16	0.247
Sinopharm	4498±1592	3934±1245	0.146	68±15	63±11	0.167
AstraZeneca		3196±659			61±12	
P value	0.00	0.00		0.61	0.84	

Discussion

By enhancing the body's natural defenses, vaccinations help people become more resistant to the virus and lessen the effects of the sickness. Therefore, it is important to evaluate the efficacy of the vaccine by evaluating the levels of markers that represent the magnitude of the immune response (CDC, 2020).

Anti-spike (IgG) levels generated against Pfizer vaccine was significantly higher than that generated against the other types of vaccines, as shown in table (2). This result is in agreement with previous study in which the author reported that the Pfizer BioNTech vaccination produce greater antibody readings after a first dose than the Oxford AstraZeneca vaccine (Eyre et al., 2021). Additionally, other study documented that comparison of ChAdOx1 (Oxford-AstraZeneca) and BNT162b2 (Pfizer-BioNTech) revealed that the mRNA vaccine BNT162b2 induces a stronger humoral response than the adenovirus-based ChAdOx1 vaccine, both after the first and second doses (Romero-Pinedo et al., 2022). Comparison of IFN γ levels among the three types of vaccines revealed no significant difference. Similarly, previous results showed that there were only marginally different variations in the cumulative number of IFN γ producing cells in participant vaccinated with mRNA (BNT162b2) and inactivated virus (Sinopharm) (Gómez de la Torre et al., 2022).

Higher antibody titter was seen in people below 25 years, as shown in table (3). The result of the current study is in agreement with previous research showed that S1 IgG levels caused by BNT162b2 immunization decreased with age, with the maximum amounts seen in people between the ages of 12 - 19(Wei et al., 2022). Also, another study documented that the geometric mean titer of anti-spike IgG was consistently lower in the older age group and declined following the second vaccination (Ikezaki et al., 2022). Inversely, Age-related differences in IgG antibody levels were evident in previous study, especially between participants in the younger (aged 21 to 30) and older age groups (Anastassopoulou et al., 2022). elderly adults are also substantially more likely to have inadequate or no post-vaccination humoral response, and the values of anti-SARS-CoV-2 antibodies after vaccination are higher than in the elderly. (Collier et al., 2021a)

With the exception of the AstraZeneca vaccine, there were no significant differences in IFN γ levels between the two age groups or within either group. However, the mean level of IFN γ for the subjects whom less than 25 years were higher than that in subjects with more than 25 years. This in agreement with previous study in which the author reported that older participants produce less IFN γ from SARS-CoV-2 spike-specific T cells than younger participants did (Collier et al., 2021b). Previous studies showed a link between the age and the potency of the humoral or cellular response (Ebersole et al., 2018). In spite of the increase in age makes the immune system suffer from characteristic changes that lead to an increase in the severity and the extent of the spread of infectious diseases, as well as to a lack of complete protection after the vaccine (Weinberger et al., 2008), But it was becoming clear that when considering the immune health, age is just a number, where age was not a measure to how well the immune system was.

There was significant difference in IgG concentration among the three types of vaccines within male and female subjects and the antibody production was higher in participants vaccinated with Pfizer, as shown in table (4). Similarly, in a previous study, where the anti-SARS-CoV-2 S1 IgG ELISA assay was used to monitor humeral response to COVID-19 mRNA BNT162b2 vaccine, did not show any statistically significant correlation between the sex of the individuals and the anti-spike protein antibody titers (Dörschug et al., 2021). Additionally, the mean value for all types of vaccines (Sinopharm, AstraZeneca, Pfizer) showed no significant differences in IgG titer for vaccinated males and females (Abdul-Ghani, 2022). Inversely, significant difference in IgG concentration between males and females was observed previously. The anti-Spike-RBD IgG response were observed to be

significantly more in females than in males after vaccination with BNT162b2 (Gharpure et al., 2021).Regarding the IFN γ, there were no significant differences neither among the three types of vaccines, nor between males and females for each vaccine despite that the mean level of IFN γ in females was higher than that in males in subjects vaccinated with Pfizer and Sinopharm. The IFN γ level was higher in males in comparison to females in subjects vaccinated AstraZeneca. Significant difference in the IFN γ levels between male and females in fully vaccinated subjects was observed by Kurteva et al., (Kurteva et al., 2022). CD4+ and CD8+ T cells in female generate more robust responses to viral infections (Raza et al., 2021). This study reported lower T cell levels in males associated with worsening disease as compared to females. Moreover, number of activated CD8 T cells were significantly higher in females (Takahashi et al., 2020). Higher activity of T cells may in turn contribute to potentially better antiviral adaptive immune response in females, which may lead to greater viral clearance. It is well established that, compared to males, females develop stronger humeral and cellular immune response to foreign antigenic stimulation, vaccination and infections than male which is considered as benefit (Fink & Klein, 2015). Whereas, strong immune response generated by females to self-antigens make them susceptible to autoimmune diseases (Klein & Flanagan, 2016).

As shown in table (5), No significant variation was observed between the first and second dose for each type of the three vaccines. However, based on the type of vaccine, significant difference was observed within each dose. The highest concentration was seen in Pfizer vaccine.

Regarding IFN γ, there were no significant difference between the first and second doses for each type of vaccines and among the first dose and second dose for all types of vaccines.

The result of the current study is in agreement with other recent study which found that the second dose of the vaccination did not improve humoral or cellular immune responses since neither anti-spike IgG levels nor specific IFN γ producing T cells significantly increased (Busà et al., 2022). In another study, stated that despite infected patients with COVID-19 showed robust humoral and antigen-specific responses to the first dose, these responses did not improve following the second dose of the vaccine at the time points examined (Samanovic et al., 2022). Tormo et al., reported that IFN γ production by T cells improved over time following the second dose, reaching levels comparable to those seen following the first dose (Tormo et al., 2022). Inversely, other study which has been done in Bagdad clarified that the second dose of vaccine caused a significant higher increase in the mean levels of IgG (29.08 ± 2.37) as compared to the mean levels (23.42 ± 1.25) of those who were administered the first dose all types of vaccine (Abdul-Ghani, 2022). The differences in the result might possibly due to time of sample collection after vaccination. It was documented that the level of IgG generated after vaccination began to decline after 60 and 120 days for Pfizer and Sinopharm, respectively. Most of the participants enrolled within this study had taken the vaccines before more than 10 weeks.

Pfizer vaccine produce higher antibody level and less IFN γ in males than females. Sinopharm vaccine produce higher antibody and IFN γ levels in females whereas AstraZeneca produce lower antibody and IFN γ levels in females. After the first dose with Pfizer and Sinopharm, antibody and IFN γ production were higher than that produced after the second dose.

Conclusion

Participants vaccinated with Pfizer vaccine produces the highest antibody and IFN γ concentration as compared to AstraZeneca and Sinopharm vaccines. Younger participants had higher antibody and IFN γ concentrations than older participants vaccinated with Pfizer and Sinopharm but not for the significant level. Regarding Sex,

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