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Evaluation of sCD4 and sCD8 in people vaccinated with Pfizer-BioNTech (BNT162b2) or Sinopharm (BBIBP-CorV)vaccine, convalescent patients and infected patients with Covid-19

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Abstract :

Introduction: The large and widespread of the SARS Covid-19 virus that the world witnessed, which claimed the lives of many people and infected millions of them, led to the rapid production of many vaccines to limit the spread of this virus, including mRNA vaccines (Pfizer) and inactivated vaccines (Sinopharm), which was used in Iraq and had an effect in reducing the spread of infections due to the effectiveness of cellular immune responses to it.

Methods: ELISA kit (elabscience company USA) for sCD4 & sCD8 as markers for cell mediated immunity was used for the subjects before the first and after the first and second dose of the Pfizer and Sinopharm vaccines, and compared with convalescent patients and patients with Covid-19.

Results: The results showed that there was a significant difference in serum soluble CD8 between the three times of sampling in the Pfizer vaccine, while Sinopharm did not show any significant difference, as for serum soluble CD4, both vaccines did not show any significant difference for the three times of sampling, but Sinopharm vaccine showed a significant difference for both factors when comparing the after the second dose with patients, and did not show any significant difference when comparing them with convalescent patients, as for the Pfizer vaccine, it did not show a significant difference for both markers with the convalescent patients and patients with the covid 19, except serum soluble CD4, which showed a significant difference with the infected patients.

Conclusion: The cellular immune response resulting from the use of Covid-19 vaccines (Pfizer or Sinopharm) is parallel to the cellular immune response resulting after recovery from infection, Also, the correlation curve between serum soluble CD4 and serum soluble CD8 of the vaccinated groups (Pfizer or Sinopharm) and convalescent patients is almost identical, and this is an indication of the efficiency of the vaccine because it gives an immune response similar to the immune response after infection.

Keywords: **covid-19, Pfizer , Sinopharm, Soluble CD4, Soluble CD8.**

تقييم sCD4 وsCD8 لدى الأشخاص الذين تم تطعيمهم بلقاح Pfizer-BioNTech و(BNT162b2) أو لقاح Sinopharm (BBIBP-CorV) ومرضى النقاهة والمرضى المصابين بـ Covid-19

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مستخلص

المقدمة: إن حجم وانتشار فيروس سارس كوفيد-19 الذي شهده العالم والذي أودى بحياة العديد من الأشخاص وأصاب الملايين منهم، أدى إلى سرعة إنتاج العديد من اللقاحات للحد من انتشار هذا الفيروس، بما في ذلك لقاحات mRNA (فايزر) واللقاحات المعطلة (سينوفارم) التي استخدمت في العراق وكان لها تأثير في الحد من انتشار العدوى بسبب فعالية الاستجابات المناعية الخلوية لها.

المواد وطرق العمل: تم استخدام مجموعة ELISA (شركة elabscience USA) لـ sCD4 و sCD8 كعلامات للمناعة الخلوية للأشخاص قبل الجرعة الأولى وبعد الجرعة الأولى والثانية من لقاحات فايزر وسينوفارم، ومقارنتها مع مرضى النقاهة والمرضى الذين يعانون من كوفيد-19.

النتائج: أظهرت النتائج وجود فرق معنوي في مستوى CD8 القابل للذوبان في المصل بين ثلاث مرات أخذ العينات في لقاح فايزر، بينما لم يظهر سينوفارم أي فرق معنوي، أما بالنسبة لـ CD4 القابل للذوبان في المصل، فلم يظهر كلا اللقاحين أي فرق معنوي بالنسبة لـ CD8 القابل للذوبان في المصل لثلاث مرات أخذ العينات، لكن لقاح سينوفارم أظهر فرقا كبيرا لكلا العاملين عند مقارنتهما بعد الجرعة الثانية مع المرضى، ولم يظهر أي فرق كبير عند مقارنتهما بالمرضى النقحين، أما لقاح فايزر فلم يظهر فرقا كبيرا لكلاهما. العلامات لدى المرضى المتعافين والمرضى المصابين بكوفيد 19، باستثناء CD4 القابل للذوبان في المصل، والذي أظهر اختلافًا كبيرًا مع المرضى المصابين.

الاستنتاج: الاستجابة المناعية الخلوية الناتجة عن استخدام لقاحات كوفيد-19 (فايزر أو سينوفارم) توازي الاستجابة المناعية الخلوية الناتجة بعد الشفاء من العدوى، كما أن منحنى الارتباط بين CD4 القابل للذوبان في المصل و CD8 القابل للذوبان في المصل للمجموعات الملقحة (فايزر أو سينوفارم) والمرضى المتعافين متطابقين تقريبا، وهذا مؤشر على كفاءة اللقاح لأنه يعطي استجابة مناعية مشابهة للاستجابة المناعية بعد الإصابة.

الكلمات المفتاحية: كوفيد-19، فايزر، سينوفارم، قابل للذوبان CD4، قابل للذوبان CD8.

Introduction

Coronavirus-2 causes a syndrome known as Severe acute respiratory syndrome-associated coronavirus-2(SARS-CoV-2) (Al-kuraishy et al.,2020), and it is a pathogen that affects several systems of the body, especially the respiratory system, in addition to other body systems, and causes various symptoms such as cough, fever, difficulty breathing, diarrhea, abnormalities in cardiac conduction, neurological deficit, muscle pain, endocrine disorders, renal failure, and etc.[Borczuk and Yantiss 2022].

Spike protein is the main feature of coronaviruses, and it came to the name because it gives a crown-like appearance [Saxena 2020], and it is a glycoprotein that has an important role in the entry of the virus into the cell [Cascella et al., 2022].

The Angiotensin-converting enzyme 2 (ACE2) receptor is one of the most important receptors which the S proteins of the coronavirus bind with it, this receptor is present in the cells of the various organs of the body, such as the lung, heart, and liver. Protein S was used in the manufacture of vaccines because it is able to generate antibodies circulating in the blood, thus preventing the entry of this virus and discouraging its reproduction[Beyerstedt et al., 2021]

In this research were studied people who vaccinated with the Sinopharm or Pfizer vaccines. The Sinopharm vaccine or BBIBP-CorV is one of the traditional inactivated whole virus vaccines[Lahiri etal., 2020] and was produced by the Beijing Institute of Biological Products; with the National Pharmaceutical Group, China[WHO, 2021] , recommended by the World Health Organization because of its efficiency in preventing disease, while the Pfizer vaccine, it is considered one of the nucleic acid vaccines, as it consists of mRNA that encodes for the mutant spike proteins of this virus and produced by BioNTech in cooperation with Pfizer and provides protection against this virus by triggering an immune response against virus spikes antigens[Khuroo etal.,2020]

T cells are among the most important immune cells that the body relies on in its response against viral infection, and it has been observed that there are differences in their types and numbers according to the stage of the disease[Erdinc et al., 2021] , in se-

vere cases of this disease, many studies found an increase in the number of CD8+ cytotoxic T cells that arget the nucleoprotein of the SARS-CoV-2 virus and a decrease in CD4+ helper T cells that stimulate B cells to produce antibodies that target various virus proteins[Cohen et al., 2021].

The CD4 and CD8 markers of T cells are present in their two states attached to the surface of T cells and in the soluble state in the blood, which originates from alternative splicing or membrane shedding, and the secretion of these soluble proteins increases as a result of the stimulation of T cells which consider as a surrogate marker of immune activation[Giblin etal.,1989; Fujimoto etal.,1984 ; Kim etal.,1991; Spronk etal.,1994].

It is worth noting that a significant increase in soluble CD4 and soluble CD8 was found in patients with various infections such as HIV and Epstein virus, in addition to various immunological diseases such as rheumatoid arthritis, SLE and other diseases [Tseng etal.,2013; Siemiątkowska etal.,2023; Sawada etal.,1993; Yoneyama etal.,1995].

Materials and Methods

Study Design

Serial blood samples were collected from people who received the vaccine against coronavirus (28 subjects who receive the Sinopharm vaccine and 18 subjects who receive the Pfizer vaccine) and according to the schedule of each vaccine from several hospitals, health centers and vaccination outlets in Baghdad Governorate for the period between the beginning of March to the end of August 2022.

All participants agreed to provide the investigator with the specimens. The ethics committee of the college of science, Mustansiriyah university approved this work (Reference. No. Bcsmu/1221/0003m), informed consent according to the declaration of Helsinki ethical principles for medical research which involving human subjects was obtained from all participants.

The first samples were collected before the vaccination process (T0), the second samples were taken 21 days after the first dose of the vaccine (T1), and the third and final samples were taken after 21 days of the second dose (T2), for comparison purposes, 20 blood samples were collected from hospital-

ized patients infected with Coronavirus (were diagnosed by PCR device) in various hospitals in Baghdad, finally, 18 samples were collected from recovered subjects of Coronavirus during the convalescence period (after a month of recovery).The vaccinated subjects who suffered from a previous infection with this disease, smokers, and subjects suffering from autoimmune diseases and chronic diseases were excluded.

The serum was separated from the blood using a 1000XG centrifuge for 15 minutes, and the sample was divided into two Eppendorf tubes and kept at -20 °C until use.

Serum concentrations of sCD4 and sCD8

The concentrations of soluble CD4 and soluble CD8 were determined using the diagnostic kit represented by the sandwich ELISA kit (Human CD4 (Cluster of Differentiation 4) ELISA kit and Human CD8 (Cluster of Differentiation 8) ELISA kit-Elabscience, Texas, USA, according to the manufacturer's instructions (Obaid, and Juma, 2016; Alfatlawi,2017) , laboratory tests were conducted in the Central Public Health Laboratories (CPHL) in Baghdad.

Statistical analysis

Statistical analysis was carried out using SPSS 20 software, and significance was calculated at $P < 0.05$ using the One-Way ANOVA Calculator for Independent Measure and expressed as (Mean±SE).

3- The results

3-1- Result of sCD8 & sCD4

This study compared the concentration of serum soluble CD8 in people before and after the first and second doses for two types of vaccine and compared it with the Convalescent and infected patients with Covid-19 at a probability level of $P < 0.05$, the results showed there were significant differences between infected patients (14.37± 1.29) ng/ml when compared with convalescent patients (10.55± 0.75) ng/ml and vaccinated people for both types of vaccines, as shown in Table 1 & 2 and figure 1 & 2(all values are expressed Mean ± SE).

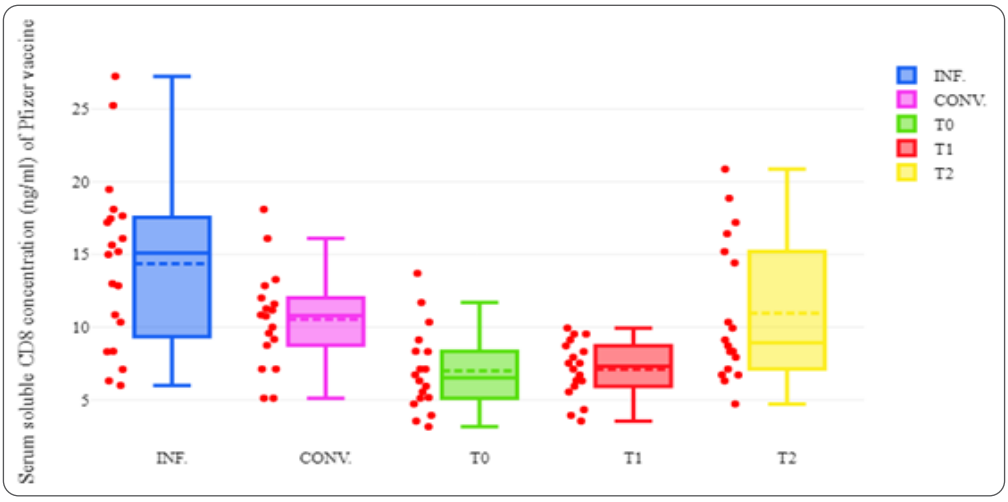
The results of the Pfizer vaccine showed a significant clear increase in the concentration of serum soluble CD8 during the vaccination stages before and after the first and second dose (6.99 ± 0.63, 7.11 ± 0.39 & 14.29 ± 2. 87) ng/ml respectively, also, there were clear statistical differences when comparing the second dose with before and after the first dose P=0.005 and P=

0.003 respectively as seen in Table 1 and Figure 1.

Table1: The Differences of serum soluble CD8 concentration before and after first and second dose of Pfizer vaccine, and convalescent and infected patient.

Doses	Serum soluble CD8 concentration of Pfizer-BioNTech (BNT162b2) (ng/ml)					
	N	Mean±SE	P-Value			
			T_0	T_1	T_2	INF.
T_0	**18**	**6.99 ± 0.67**				
T_1	**18**	**7.11 ± 0.45**	**0.89**			
T_2	**18**	**10.96 ± 1.14**	**0.005****	**0.003****		
INF.	**20**	**14.37± 1.29**	**0.00002****	**0.00001****	**0.06**	
Con.	**18**	**10.55± 0.79**	**0.001****	**0.0006****	**0.77**	0.02*
P-Value	**0.0001****					

INF. – infected patients / CONV.- convalescent patients / T0-before vaccine / T1 - after first dose / T2- after second dose (P-value < 0.05).



INF. - Infected patients/ CONV. - Convalescent patients /T0 - before vaccine / T1 - after first dose / T2- after second dose/Dashed lines mean the mean/Continuous lines mean median.

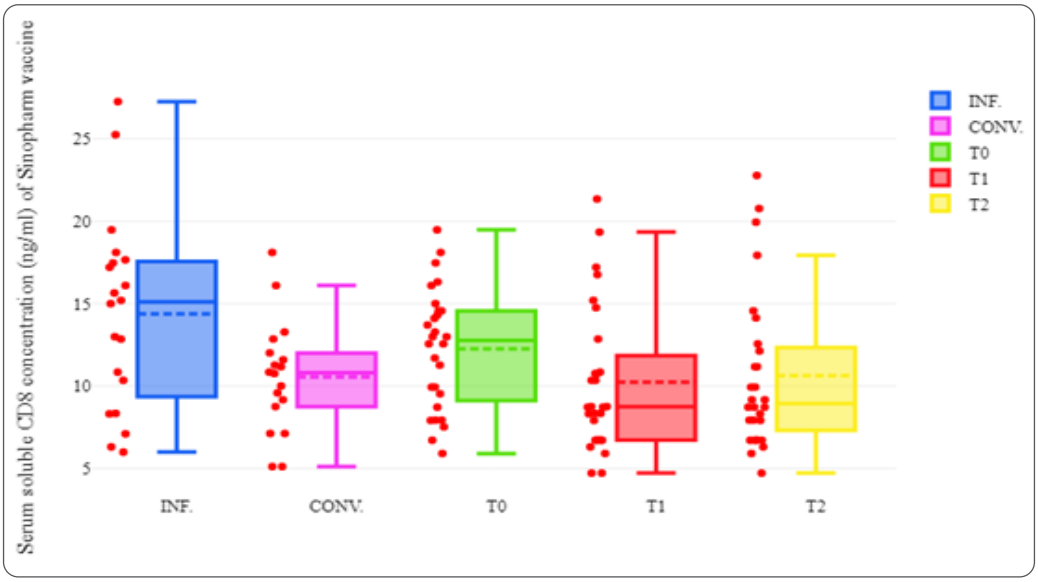
Figure 1:- comparison of serum soluble CD8 concentration between different doses of Pfizer-BioNTech (BNT162b2) vaccine with convalescent and infected patients.

While the three doses of Sinopharm vaccine did not show any significant differences between them(12.25± 0.66, 10.25± 0.8 & 10.62± 0.87) as shown in Table 2 and Figure 2.

Table2: The Differences of serum soluble CD8 concentration before and after first and second dose of Sinopharm vaccine, and convalescent and infected patients

Doses	Serum soluble CD8 concentration of Sinopharm (ng/ml)					
	N	**Mean±SE**	P-Value			
			T_0	T_1	T_2	INF.
T_0	**28**	**12.25± 0.68**				
T_1	**28**	**10.25± 0.82**	**0.06**			
T_2	**28**	**10.62± 0.89**	**0.15**	**0.75**		
INF.	**20**	**14.37± 1.29**	**0.12**	**0.007****	**0.018***	
CON.	**18**	**10.55± 0.79**	**0.11**	**0.8**	**0.95**	0.02*
P-Value	**0.01****					

INF. – infected patients / CONV.- convalescent patients / T0-before vaccine / T1 - after first dose / T2- after second dose (P-value < 0.05).



INF. - Infected patients/ CONV. - Convalescent patients /T0 - before vaccine / T1 - after first dose / T2- after second dose/Dashed lines mean the mean/Continuous lines mean median.

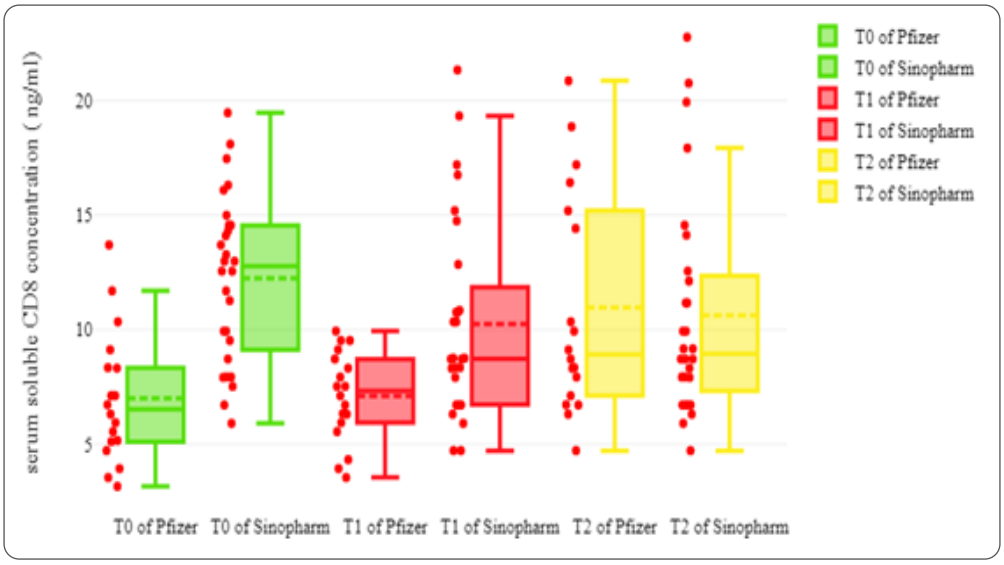
Figure 2:- comparison of serum soluble CD8 concentration between different doses of Sinopharm (BBIBP-CorV) vaccine with convalescent and infected patients

And when comparing the two vaccines during the three stages of vaccination, it was noted that there was a significant difference before and after the first dose, and there was no significant difference between the two groups after the second dose as shown in table 3 and Figure 3.

Table3: The Differences of serum soluble CD8 concentration between two types of vaccine in different time

Doses	Serum soluble CD8 concentration (*n*g/ml)				P-value
	Pfizer-BioNTech (BNT162b2)vaccine		***Sinopharm (BBIBP-CorV) vaccine***		
	N	**Mean±SE**	**N**	**Mean±SE**	
T_0	**18**	**6.99 ± 0.67**	**28**	**12.25± 0.68**	0.00001**
T_1	**18**	**7.11 ± 0.45**	**28**	**10.25± 0.82**	0 .007**
T_2	**18**	**10.96 ± 1.14**	**28**	**10.62± 0.89**	0.81
P-value	**0.001****		**0.18**		

*T0-**b**efore vaccine / T1 - after first dose / T2- after second dose (P-value < 0.05)*



T0 - before vaccine / T1 - after first dose / T2- after second dose/ Dashed lines mean the mean/Continuous lines mean median

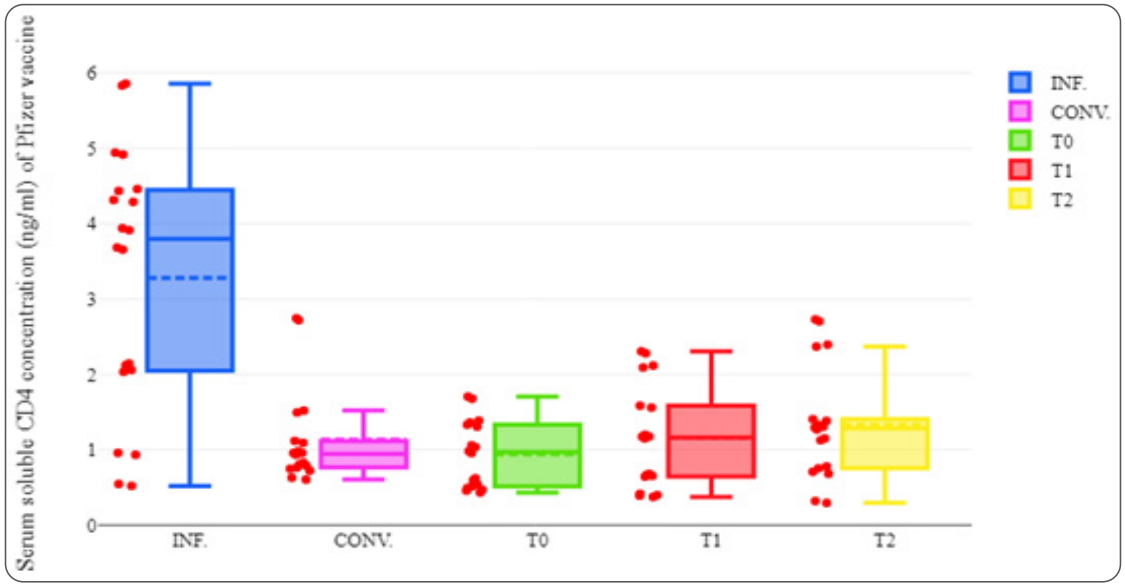
Figure 3: The Differences of serum soluble CD8 concentration (ng/ml) between two types of vaccine in different time.

This study also compared the concentrations of serum soluble CD4 in immunized subjects before and after the two doses of both vaccines, and also the above was compared with that of Convalescent patients and those who were infected with Covid-19 at P< 0.05, as tables 4 and 5, there was a significant increase in serum soluble CD4 concentration in the group of patients (3.24 ± 2.06) ng/ml compared to the group of convalescent patients (1.13 ± 0.15) ng/ml and compared with the three stages of immunization for both vaccines.

Table4: The Differences of serum soluble CD4 concentration before and after first and second dose of Pfizer vaccine, and convalescent and infected patients.

Doses	sCD4 concentration (ng/ml) of Pfizer-BioNTech (BNT162b2)					
	N	Mean±SE	P-Value			
			T_0	T_1	T_2	INF.
T_0	**18**	**0.94 ± 0.1**				
T_1	**18**	**1.16 ± 0.16**	**0.26**			
T_2	**18**	**1.33 ± 0.17**	**0.064**	**0.47**		
INF.	**20**	**3.28 ± 0.38**	**0.00001****	**0.00002****	**0.00008****	
CONV.	**18**	**1.13 ± 0.15**	**0.29**	**0.91**	**0.4**	0.00001**
P-Value	**0.00001****					

T0 - before vaccine / T1 - after first dose / T2- after second dose/ INF. - Infected patients/ CONV. - Convalescent patients / (P-value < 0.05).



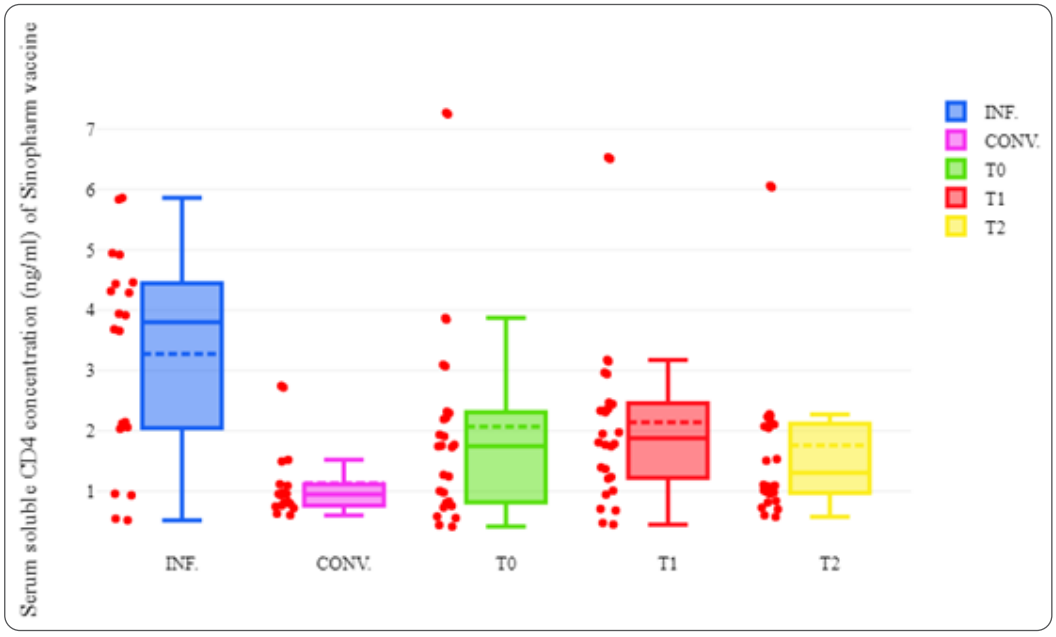
INF. - Infected patients/ CONV. - Convalescent patients /
T0 - before vaccine / T1 - after first dose / T2- after second dose/
Dashed lines mean the mean/Continuous lines mean median.

Figure 4:- comparison of serum soluble CD4 concentration between different doses of Pfizer-BioNTech (BNT162b2) vaccine with convalescent and infected patients.

Table5: The Differences of serum soluble CD4 concentration before and after first and second dose of Sinopharm vaccine, and convalescent and infected patients.

Doses	sCD4 concentration (ng/ml) of Sinopharm (BBIBP-CorV)					
	N	Mean±SE	P-Value			
			T_0	T_1	T_2	INF.
T_0	**28**	**2.07 ± 0.33**				
T_1	**28**	**2.14 ± 0.27**	**0.85**			
T_2	**28**	**1.76 ± 0.25**	**0.46**	**0.3**		
INF.	**20**	**3.28 ± 0.38**	**0.02***	**0.02***	**0.001****	
CONV.	**18**	**1.13 ± 0.15**	**0.03***	**0.008****	**0.07**	0.00001**
P-Value	**0.0004****					

T0 - before vaccine / T1 - after first dose / T2- after second dose/ INF. - Infected patients/ CONV. - Convalescent patients / (P-value < 0.05).



INF. - Infected patients/ CONV. - Convalescent patients /T0 - before vaccine / T1 - after first dose / T2- after second dose/Dashed lines mean the mean/ Continuous lines mean median.

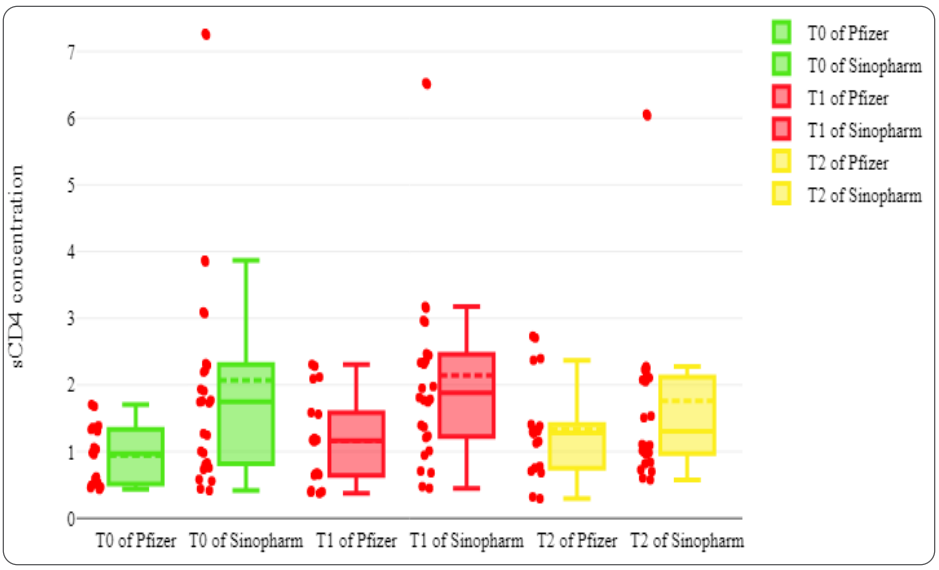
Figure 5:- comparison of serum soluble CD4 concentration between different doses of Sinopharm (BBIBP-CorV) vaccine with convalescent and infected patients

From Table 6, there were no significant differences between the three stages of the two vaccines, as well as the absence of a significant difference between Pfizer and Sinopharm in the two stages which are before vaccination and the second dose of vaccination, while there was only a significant difference after the first dose between two vaccines.

Table6: The Differences in serum soluble CD4 concentration between two types of vaccines in different time

Doses	Serum soluble CD4 concentration (*n*g/ml)				P-value
	Pfizer-BioNTech (BNT162b2)		**Sinopharm (BBIBP-CorV)**		
	N	**Mean±SE**	**N**	**Mean±SE**	
T_0	**18**	**1.273 ± 0.283**	**28**	**2.068 ± 0.331**	0 .09
T_1	**18**	**1.159 ± 0.162**	**28**	**2.145 ± 0.277**	0 .01*
T_2	**18**	**1.334 ± 0.178**	**28**	**1.758 ± 0.255**	0.23
P-value	**0.843**		**0.608**		

T0-before vaccine / T1 - after first dose / T2- after second dose (P-value < 0.05).



T0 - before vaccine / T1 - after first dose / T2- after second dose/ Dashed lines mean the mean/Continuous lines mean median.

Figure 6: The Differences of sCD4 concentration (pg/ml) between two types of vaccine in different time.

The results of the infected and convalescent were compared with the three doses of the two vaccines, as in Tables 1, 2, 3 and 4 what matters to us is the post-vaccination results (after the second dose), it was noted that there was no significant difference between the recovered and this stage of the vaccine result of the two vaccines and this is the important point of the study.

3-2- The correlation between sCD4 and sCD8 concentration

Correlation between sCD4 and sCD8 in groups of vaccinated subjects with Sinopharm or Pfizer, Convalescent patients and infected patients were analyzed with the Spearman rank correlation coefficient, where Sinopharm vaccine and convalescent patients indicated that there is a significant large positive relationship between sCD8 and sCD4 ($r= 0.605$, $p < 0.001^{**}$), ($r= 0.656$, $p = 0.003^{**}$) respectively, while Pfizer vaccine indicated that there is a significant medium positive relationship between sCD8 and sCD4 ($r = 0.49$, $p = 0.04^{*}$),and infected patients indicated that there is a non-significant very small positive relationship between sCD8 and sCD4 ($r = 0.0571$, $p = 0.755$), as shown in figure 7.

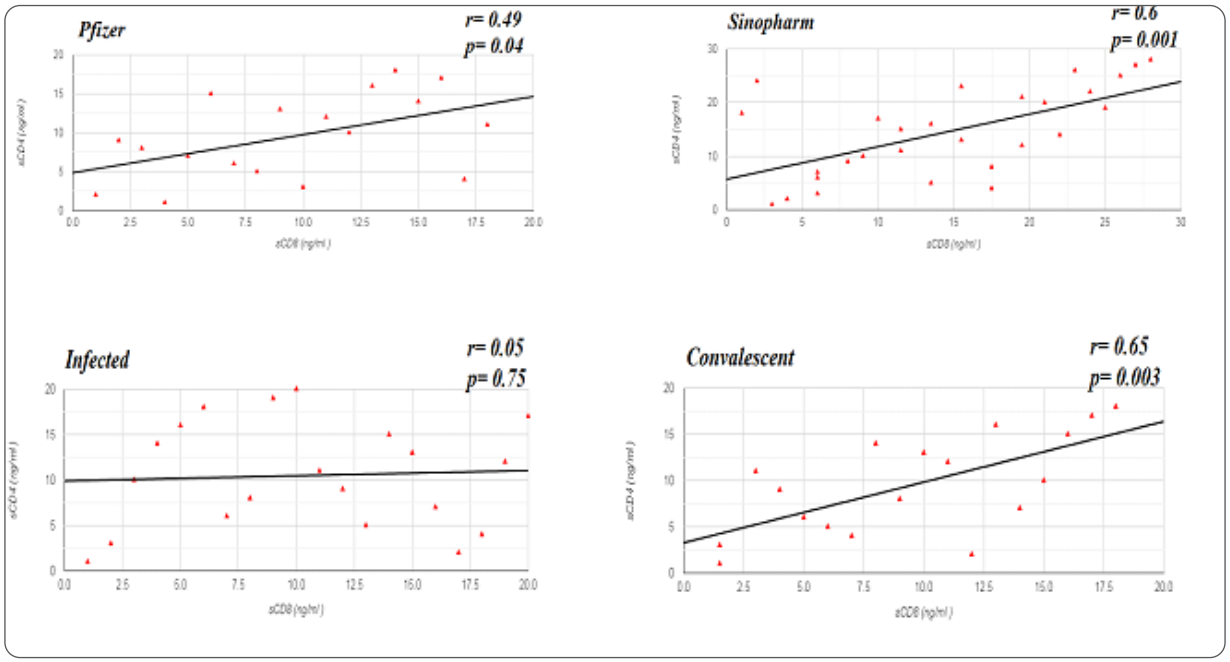


Figure 7:- the correlation between scd4 and scd8 in vaccinated subjects (Pfizer or Sinopharm), convalescent and infected patients.

4- Discussion

An old in vitro study dating back to 1983 showed that CD8 antigen is spontaneously secreted from CD8 + leukaemic cells and its concentration increases according to the increase in the activation of CD8 T cells[Fujimoto etal.,1983]. In 1989, Tomkinson and his colleagues devised a method for measuring CD8 through the ELISA technique, where they indicated that there is soluble CD8 produced by stimulated lymphocytes as a result of the immune response to EBV infection, which as a result gives an indication of an increase in CD8 cells [Tomkinson etal.,1989] , Nishanian and his colleagues found in 1991 that this marker gives the predictive subsequent of the onset of AIDS[Nishanian etal.,1991], the same applies to CD4, which is elevated in AIDS patients[Reddy et al., 1990], while it is normal in the serum of healthy individuals [Kline et al., 1989] and the ELISA method is one of the cheap ways to check for this marker.

The concentration of sCD4 and sCD8 in the serums of the studied groups gives us a description of the immune status of these groups. The cellular immunity represented by T cells, whether CD8 or CD4, are factors to eliminate virus-infected cells during various virus infections, there have been many studies on the role of these cells in SARS-CoV-2 infection, as they limit the severity of the disease [Song etal.,2020; Zheng etal.,2020; Liao etal.,2020; Ganji etal.,2020].

Both vaccines used are considered multivalent SARS-CoV-2 vaccines because they provide protection against different strains of this virus due to contain different antigenic determinants for different variants that can generate a strong immune response against the new variants as a result of the cross-reaction of the immune response [Ghazvini and Keikha 2023], and multiple doses of these vaccines stimulate long-term cellular immunity through immune memory T-cells specific to this virus, as we mentioned earlier, T cells play an important role in both responses humoral and cellular immunity, as Zhang and his colleagues recommended 2022 to study the cellular immune response that induced by inactivated vaccines after they studied and found the effective role of humoral immunity for this vaccine[Zhang etal.,2022].

The results showed that there was no significant difference in the con-

centration of serum soluble CD4 between the immunization stages of both vaccines, while serum soluble CD8 showed a clear significant difference between the immunization stages of the Pfizer vaccine, and there was a clear gradual rise in the concentration of serum soluble CD8, and this result is clearly explained because the immune response against any viral infection through activate and a steady increase of CD8 cells, while the results of the Sinopharm vaccine were not as in the Pfizer vaccine, because there was no significant difference in the concentration of this factor between the three stages of Sinopharm vaccination, and this is due to various reasons, including the quality of the vaccine that depends on various factors, the most important of which is the method of vaccine storage and the difference in the immune status of the vaccinated people, where it was noted that the concentration of serum soluble CD8 was higher before the immunization process than after the first and second stages of vaccination however, a slight increase in the serum soluble CD8 concentration was observed after the second dose compared with after the first dose, with regard to the Pfizer vaccine, our study confirmed the results obtained by Oberhardt and his colleagues in 2021, where an expansion in the CD8 cell clonal as a result of vaccination with the Pfizer vaccine, while CD4 cells were weakly detectable[Oberhardt etal.,2021], and Sato and his colleagues 2022 confirmed that CD4 cells are convergent level before and after vaccination with the Pfizer vaccine[Sato etal.,2022], and this was confirmed by our current study regarding this type of cells in people vaccinated with the Pfizer vaccine, while a Saudi study by Alsayb and his colleagues 2021 showed an increased level of CD4 cells in those who recovered from Covid-19 disease when compared to healthy people, and there was no significant difference in CD8 cells between the recovered group and the uninfected control group[Alsayb etal.,2021].

As for the Sinopharm vaccine, our results showed a non-significant decrease in serum soluble CD4 and serum soluble CD8 between the three doses. Fu and colleagues 2021 found a slight, non-significant increase in CD4 and a significant increase in CD8 when using inactivated vaccines, which he stressed in his discussion on activating the response of T cells to various vaccines

by reviewing other research, especially CD8 cells, and this may contradict the results obtained and this may be due to many reasons, including the time of taking the sample and the environmental conditions surrounding conducting the tests and the nature of the immune response of the people participating in this study and etc. [Fu etal.,2021].

The study of Ben Ahmed and his colleagues 2022 showed that the immune response to the Pfizer vaccine was higher than that of Sinopharm for CD4 and CD8, while our study showed for the third dose of two vaccines there was a non-significant increase in sCD8 for the Pfizer vaccine compared to the Sinopharm vaccine, as for sCD4 there was a non-significant increase in Synopharm compared to Pfizer vaccine [Ben Ahmed etal.,2022].

What interests us in this study is the results of the third stage, which represents the final outcome of the vaccination process, as we did not notice a significant difference between the Sinopharm and Pfizer vaccines for both serum soluble CD4 and serum soluble CD8 table 3 & 6. The previous studies have emphasized the importance of conducting research on this topic to confirm the importance of the effectiveness of the vaccination process, and Galvan and Quarleri 2022 through their review confirmed the role of the target of the vaccine used, as there are single-target vaccines that target spike proteins such as the Pfizer vaccine and vaccines that target several proteins of the virus, such as Sinopharm, it is axiomatic that the vaccine with multiple targets is better because it can give an immune response against mutant strains, as well as the role of adjuvants used with vaccines that have a role in enhancing the adaptive immune response of all kinds [Galvan, V. and Quarleri, J., 2022].

What confirms the validity of our results is the presence of the two groups of convalescent patients and patients infected with Covid-19, where we notice a significant increase in these two markers in the group of patients compared to the convalescent patients and vaccinated patients after the third dose.

Knowing that this study faced difficult challenges in dealing with vaccinated people, the most important of which is their lack of commitment to giving blood samples after the vaccination stages, as they were excluded from this study, and if the number was more than the participants, there would have

been more controlled results, and for this we recommend conducting more studies on this topic that may support this results.

As it is known that the cellular immune response in all its forms is dependent on T cells CD4 through the interference of its receptors with antigen-presenting cells through MHC II, which stimulate CD8 cells and B cells, as well as their ability to produce cytokines, which are considered as signals employed to recruit various immune cells, thus, we note from the figure? for the three groups vaccinated with the Pfizer or Sinopharm vaccines and the Convalescent patients that there is a significant positive relationship between sCD4 and sCD8, this indicates that the immune response resulting from the two vaccines is parallel to the immune response that occurs after infection figure 1, while we note that the infected subjects have a non-significant positive relationship between these two factors and in this group, there are several factors that control this result, the most important of which are the stage of the disease, the severity of the infection, and the immune status of the infected subject, as Boechat and his colleagues 2021 indicated that the acute stage of this disease is characterized by high activity of cytotoxic T cells, while in Convalescent patients is characterized by polyfunctional T cells are predominant. This contradicts Grifoni, and his colleagues 2020, who found that there is a significant positive relationship between serum soluble CD4 and serum soluble CD8 in patients with Covid-19, and he justified this by not knowing which of the virus antigens will be targeted by different immune cells, which will determine the type of immune response against this virus.

Conclusion: The cellular immune response resulting from the use of Covid-19 vaccines (Pfizer or Sinopharm) is parallel to the cellular immune response resulting after recovery from infection, Also, the correlation curve between serum soluble CD4 and serum soluble CD8 of the vaccinated groups (Pfizer or Sinopharm) and convalescent patients is almost identical, and this is an indication of the efficiency of the vaccine because it gives an immune response similar to the immune response after infection.

Recommendation:- Our current study recommended the importance of vaccination in reducing SARS-CoV-2 infection, and that the effect resulting

from vaccination does not have any adverse effects on healthy subjects as in the case of illness. what matters to us is the post-vaccination results (after the second dose), it was noted that there was no significant difference between the recovered and this stage of the vaccine results of the two vaccines therefore this study is recommended to the importance of the second dose of any vaccine, and this is the important point of the study.

Institutional Review Board Statement: written consent was obtained for all participants in this study according to the ethics committee of the College of Science, Mustansiriyah University approved this work (Reference. No. BCSMU/1221/0003M), according to the declaration of Helsinki ethical principles for medical research which involving human subjects.

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