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Biochemical Action of Vaccines in Iraqi Patients with COVID-19 Infection

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Abstract

The aim of the present study is to compare the biochemical action of the three vaccines taken in Iraq: Pfizer Biontech, AstraZeneca Oxford and Sinopharm based on biochemical parameters. Seventy COVID-19 Iraqi patients (males and females) were participated in the present study and classified into 7 groups : Gc : COVID-19 patients (without vaccine) , Gp_1: COVID-19 patients took one dose of Pfizer Biontech, Gp_2 : COVID-19 patients took two doses of Pfizer Biontech, Ga_1 : patients took one dose of AstraZeneca Oxford vaccine , Ga_2: patients took two doses of AstraZeneca Oxford vaccine , Gs_1 : patients took one dose of Sinopharm vaccine and Gs_2: patients took two doses of Sinopharm vaccine. Patients were compared with healthy subjects (without vaccine) as a control group (Gh). The D-dimer level was highly significantly increased in Gc compared with Gh and was highly significantly decreased in Gp_1 , Ga_1 , Ga_2 , significantly decreased in Gp_2 and non-significantly decreased in Gs_1 and highly significant increased in Gs_2 compared with Gc. CRP level was significantly increased in Gc compared with Gh while it was significantly decreased in Gp_1, Gp_2, Ga_1 , Ga_2 , Gs_1 , Gs_2 compared with Gc. IgG and IgM levels were increased in Gc but decreased after taking vaccines (except Ga_2 for IgG and Gp_2 for IgM) The present study submits a novelty to the field of COVID-19 by highlighting the chemical aspects of vaccines used in Iraq

Keywords: AstraZeneca Oxford. COVID-19. C-reactive protein. D-dimer. Immunoglobulin G . Pfizer Biontech.

Introduction

At the end of 2019 , a newly diagnosed coronavirus named (SARS-CoV-2 virus) has invaded and caused COVID-19 infections , its outbreak began in China and developed quickly to be declared by the world health organization (WHO) as a dangerous pandemic in March 2020.[1] Medically , Coronavirus disease (COVID-19) is caused by a novel strain of coronavirus 2 called as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[2] COVID-19 infection is mostly featured by difficulty breathing , fever and headache and is associated with many complications which resulted in severe fatigue leading to hospital and admission and sometimes uncontrolled cases developed into death.[3] Coagulation or coagulopathy plays a pivotal role for COVID-19 patients.[4,5] D-dimer is a small protein (180,000 Da) as the final product (fragment) of cross linked fibrin degradation mediated by plasmin, its level in blood depends on clotting activation accompanied by fibrin production, stabilization by factor XIIIa, and next degradation by the endogenous fibrinolytic system.[4] Generally, the inflammatory responses are the major clinical feature during COVID-19 infection.[5] C-reactive protein (CRP) is the first and most common protein described as the sensitive and ideal biochemical marker of

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inflammation and tissue damage , CRP belongs to protonic pentraxin family which seems as 1000-fold or more level increasing during injury , inflammation and tissue damage.[6] If the systemic inflammation increased in severe cases of COVID-19 , anti-SARS-CoV2 IgG and IgM level is increased in patients blood.[7] Despite the safety and effectiveness of a number of novel vaccines ,[1] mutations of different strains of this virus result in new waves of appearance which cause partial vaccine resistance.[3] COVID-19 vaccines admitted and confirmed by World Health Organization (WHO) play a great role by supporting the immune system to fight pathogens via releasing specialized immune responses. COVID-19 vaccines consist of weak or killed forms of this virus which retain its ability to activate the immune system of the person receiving it to produce antibodies (immunoglobulins) and specialized white blood cells called (T-cells), the result is recognizing the virus, fighting and destroying it. Indeed, it takes several weeks after taking vaccines for the body to produce these antibodies and T-cells.[1] Pfizer Biontech, AstraZeneca Oxford and Sinopharm were the major introduced and popular vaccines in the world. Regardless of the partial activity and the side effects, vaccines are the only and the best way to overcome COVID-19.[8] and reduce its risk. Moreover , wearing masks and using alcoholic sterilizers besides social distancing aid in controlling the disease spread.[3] Remarkably , the headlines of most previous and recent studies regarding COVID-19 focused on the medical features of not vaccinated subjects or the adverse effects of vaccine for vaccinated subjects (pain , fever , vomiting) but limited studies dealt with biochemical parameters and in particular their relationship with vaccines , consequently , the aim of the present study is to compare the biochemical action of the three vaccines taken by COVID-19 patients in Iraq : Pfizer Biontech, AstraZeneca Oxford and Sinopharm vaccine) by highlighting four biochemical parameters : D-dimer , C-reactive protein , Immunoglobulin G and Immunoglobulin M.

Materials and Methods

Patients' selection and study protocol

Seventy COVID-19 Iraqi patients were enrolled in the present study, they were newly diagnosed by polymerase chain reaction (PCR) as COVID-19 patients after attending a number of private laboratories and institutes in Iraq / Baghdad. Anyway, this study involved patients from two genders (males and females), a large number of them took vaccine (one dose or two doses before being infected) Interestingly, taking vaccines provoked a motive for me to organize the study protocol according to whether the patient took or didn't take the vaccine, number of doses and the vaccine type for patients who took the vaccine. Remarkably, all groups in table 1 except Gh were infected with COVID-19. Honestly, I collected blood samples from all COVID-19 patients I have met in a number of Baghdad clinics and private laboratories and divided them into groups based on taking and not taking vaccines, vaccine type and doses (I exclude patients suffering from other chronic or inflammatory diseases and also patients under treatment because this may interfere with results and minimize accuracy of biochemical measurements.). Accordingly, patients were classified into seven groups: Gp_1, Ga_1 and Gs_1 are subjects who took the first dose of the vaccine before being infected while Gp_2, Ga_2 and Gs_2 are other subjects who took two doses of the vaccine before being infected as shown in table 1, the time between the two doses is between 25 to 35 days for patients who took the two doses of the vaccine. Patients were compared with healthy subjects Gh (males and females) as a control group, in ages matched with patients. Interestingly, Gh is the same control group for all types of vaccination. Importantly, the study protocol was based on the biochemical action of the vaccines taken in Iraq (types and doses) and not includes the variation between the sexes for two reasons Firstly: no statistical difference was found between males and females and secondly: the aim of the present study focused on the biochemical action of the three vaccines (including vaccine types and doses) regardless sex.

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Table 1. The study protocol regarding number, age , sex, taking vaccine, vaccine type and number of doses.

Group	Number	Age	Sex	Clinical status regarding vaccine
Gh	10	46±2	Males and females	**Healthy control subjects (without vaccine)**
Gc	10	47±2.2	Males and females	**COVID-19 patients (without vaccine)**
Gp_1	12	44±3.3	Males and females	**COVID-19 patients took one dose of Pfizer Biontech vaccine**
Gp_2	12	41±1.1	Males and females	**COVID-19 patients took two doses of Pfizer Biontech vaccine**
Ga_1	10	47±1.3	Males and females	**COVID-19 patients took one dose of AstraZeneca Oxford vaccine**
Ga_2	8	47±1	Males and females	**COVID-19 patients took two doses of AstraZeneca Oxford vaccine**
Gs_1	10	32±1.3	Males and females	**COVID-19 patients took one dose of Sinopharm vaccine**
Gs_2	8	33±1.1	Males and females	**COVID-19 patients two doses of Sinopharm vaccine**

Blood sampling

Ten milliliters of venous blood were collected from each subject enrolled in the present study , sera were separated from blood cells by centrifugation for 5 minutes at 4000 round / minute , the resulted serum from each subject was divided into four small portions (each put inside an eppendorf) and kept frozen at -20°C until performing biochemical laboratory analysis which conducted in the international center for research and development (ICRD) / Baghdad .

Biochemical Analysis

D-dimer was determined on the basis of quantitatively ELISA method. In particular, the human D-dimer solid phase sandwich enzyme-linked immunosorebent assay is designed to detect the amount of the target bound between the matched antibody pair. According to the present study, a target antibody was pre-coated on each well of the provided microplate. Hence, samples and standards were added to wells and bound with the immobilized (capture) antibody. Subsequently, the sandwich was formed by the addition of another antibody, then a substrate solution was added and reacted with the enzyme – antibody –target complex to give detectable signal whose intensity was directly proportional with the target concentration found in the original specimen (serum). C-reactive protein (CRP) was determined by nepheometric rapid quantitative test (Nepheometric test is used to evaluate the presence and severity of inflammation in the body), this test is a specific type of neplelometry used to measure the concentration of CRP in a patients' blood sample. It involves mixing the patients' sera with a reagent that causes any CRP present in the serum to bind with latex particles, blood sera were mixed with intralipid 20% (which contains 1.2% egg yolk phospholipids) in Tris-calcium buffer, after incubation 10-12 min at 37°C. Subsequently, these CRP- latex complexes cause light to scatter, which is measured by a nephelometer. The amount of scattered light is directly proportional to the concentration of CRP in the blood sample, CRP phospholipid complexes were detected by nepheometry. This laboratory test is quick and accurate. Regarding virology aspect, COVID-19 antibodies (IgG) and (IgM) were determined by chemiluminescence Immunoassay, this test is a quantitative serological antibody detection assays which have high sensitivity and specificity. The continuous determination of antibodies concentrations could be used to assess the progression of COVID-19 cases. The amount of IgG and IgM was positively correlated with the relative light units (RLU) measured by the chemiluminescence analyzer and specifically detected by the iFlash optical system. Anyway, chemiluminescence is preferred because it uses a simple device and also allows the process to have a wide dynamic range detecting light from binding events whether the sample is diluted or concentrated.

Statistical Analysis

Student T test in the term of probability (p) was applied to compare the difference between values resulting from each group. When p value ≤ 0.05, the

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difference is regarded as significant, when p value ≤ 0.001, the difference is regarded as highly significant and when p value > 0.05, the difference is regarded as non-significant.

Results and Discussion

Results of the present study have reported that D-dimer level (ng/mL) was highly significantly increased in sera of Gc (865.5±11.05) compared with Gh (282±5.40). In contrast , it was highly significant decreased in sera of Gp_1 (338.5±9.1) , Ga_1(290±2.3) , Ga_2 (348.8±103.1) , significantly decreased in Gp_2 (432±19.8) , and non-significantly decreased in Gs_1 (568±25.2) and highly significant increased in Gs_2 (2107.6±1192.9) compared with Gc (865.2±11.02) ng/mL. The difference between Gp_1 (338.5±9.1), Gp_2 (432.6±19.8), Ga_1 (290.4±2.3) Ga_2 (348.8±103.1) and Gh (282±5.40) was non-significant while the difference between Gs1 (568.7±25.2) and Gh (282±4.5) was significant, and the difference between Gs_2 (2107.6±1192.9) and Gh (282±5.40) was highly significant, table 2. Regarding CRP (mg/dL), results of table 3 have shown that CRP level was significantly increased in sera of Gc (59.07±5.8) mg/dL compared with Gh (4.80±1.22). On the other hand, CRP level (mg/dL) was significantly decreased in sera of Gp_1 (7.15±1.71), Gp_2 (7.96±0.68), Ga_1 (5.46±2.42) mg/dL, Ga_2 (5.44±1.75), Gs_1 (2.45±1.31), Gs_2 (5.39±1.92) compared with Gc (59.05±5.80). The difference between Gp_1 (7.15±1.71), Ga_1 (5.46±2.42), Ga_2 (5.44±1.75), Gs_2 (5.39±1.92) and Gh (4.80±1.22) was non-significant, while the difference between Gp_2 (7.96 ±0.68), Gs_1 (2.45±1.31) and Gh (4.60±1.22) was significant. According to IgG level (mLU/mL), it was significantly increased in sera of Gc (6.72±2.18) compared with Gh (0.43±0.28) while it was non-significantly decreased in Gp_1 (5.04±0.85), Gp_2 (5.20±0.70), Ga_1 (6.11±0.83), Gs1 (4.81±1.12) and significantly decreased in Gs_2 (1.86±0.62) compared with Gc (6.72±2.18). Remarkably, IgG level was highly significantly increased in Ga_2 (22.00±1.60) compared with Gc (6.72±2.18). The difference between Gp_1 (5.04±0.85), Gp_2 (5.20±0.70), Ga_1 (6.11±0.83), Ga_2 (22.00±1.60), Gs_1 (4.81±1.12) and Gh (0.43±0.28) was highly significant while the difference between Gs_2 (1.86±0.62) and Gh (0.43±0.28) was significant, table 4. Moreover, IgM level (mLU/mL) was highly significant increased in sera of Gc (1.48±0.47) compared with Gh (0.55±0.28) table 5, while it was highly significant decreased in Gp_1 (0.553±0.462) and highly significant increased in Gp_2 (2.97±0.27) and non-significantly decreased in Ga_1 (1.36±0.65), Ga_2 (1.15±0.08), Gs_1(1.09±0.39) and Gs_2 (1.33±1.70) compared with Gc (1.48±0.47). The difference between Gp_2 (2.97±0.27) and Gh (0.55±0.28) was highly significant while the difference between Ga_1 (1.36±0.65) Ga_2 (1.15±0.08), Gs_1 (1.09±0.39), Gs_2 (1.33±1.70) and Gh (0.551±0.28) mLU/mL was significant and the difference between Gp_1 (0.553±0.462) and Gh (0.55±0.28) was non-significant.

D-dimer and CRP are the most biochemical markers linked with coronavirus disease 2019 (COVID-19).[5,9] D-dimer blood levels depend on coagulation activation with fibrin generation caused by that D-dimer is the final product of plasmin mediated generation of fibrin.[4] Hence , a recent study has shown that coagulation and the mammalian immune system are directly linked via the activation of interleukin-1α by thrombin (the key enzyme for coagulation).[10] Interestingly , the major coagulation is contributed by immune cells (monocytes and neutrophils) and also cytokines (mostly secreted by leukocytes) plays a key role in coagulation process.[11] Generally, Blood coagulation is activated during infection and components of the hemostatic system are definitely involved in the immune responses and modulation,[12] this is why D-dimer level was highly significant in Gc compared with Gh (big gap between Gc and Gh), table 2. However, the activation of coagulation has a great role in virus infections by limiting pathogen dissemination and enhancing pathogen killing and tissue repair but over activation causes thrombosis. Besides D-dimer, CRP also plays a great role regarding immune system, CRP represents the principal downstream mediator of the acute phase response following an inflammatory

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status.[13,14] It is biosynthesized basically in liver in the presence of interleukin-6 [15] Moreover , CRP is also expressed by human respiratory epithelial cells , alveolar macrophages and monocytes , suggesting its pivotal role in immune defense and responses,[6] this is why CRP was significantly increased in Gc compared with Gh (the big gap between Gc and Gh is reflected by the higher inflammatory status caused by COVID-19 because cases with other chronic and inflammatory diseases were excluded). It has been concluded that D-dimer and CRP are the immune aspects in the term of COVID-19. Definetly, IgG and IgM levels were increased in Gc compared with Gh as a response to the inflammatory status caused by the immune system alterations by corona virus.[7] but the increase was significant for IgG and highly significant for IgM. Remarkably, potassium derivatives (potassium phosphate and potassium chloride) are control parameters (basic biochemical parameters) within Pfizer Biontech COVID-19 vaccines.[16] Potassium derivatives prevalence in this vaccine gives a hint for potassium role regarding COVID-19. In this regard, a recent study has reported that potassium influx plays a contributed role in immunological responses and potassium deficiency in serum may be linked with innate immune system.[17] In accordance with SARS-CoV infection, lower levels of potassium are caused by higher levels of aldosterone which enhances excretion of potassium in urine. It has been suggested that potassium dysregulation in a part of the mechanism by which viral pathogenicity is promoted and the role of vaccine in reducing COVID-19 infection severity via the interaction with the immune system.[18] This is matched with Pfizer Biontech caused by the presence of potassium derivatives as control parameters. The present study is the first providing insights for Pfizer Biontech function in the term of its chemical structure. Interestingly, immune system plays the greatest role in the term of COVID-19 disease because SARS-CoV infection results in a range of features from mild pneumonia to cardiac arrhythmias, hyperactivation of the immune responses, systemic organ failure and death.[18] This is why D-dimer and CRP levels were decreased in Gp1 and Gp2 compared with Gc. Anyway, the degree of statistical difference was controversial among groups regarding dose numbers. According to D-dimer, the significant decrease in Gp2 compared with Gc versus the highly significant difference in Gp1 compared with Gc may be due to the severity of infection for subjects of Gp2 and the few numbers of persons within the group. However, Pfizer Biontech was great for shifting D-dimer towards balance caused by the difference between Gp1, Gp2 and Gh was non-significant, table 2 . However, data related to CRP was very good reporting significant decrease in Gp1 and Gp2 compared with Gc and non-significant difference between Gp1 and Gh, table 3. COVID-19 virus has inside its envelope a spike protein targets angiotensin-converting enzyme-2(ACE-2) receptors to enter and be propagated in the cells,[11] ACE2 is expressed in a number of human tissues and organs.[19] Endothelial cells in pulmonary vasculature, coronary circulation , cerebral circulation and intestinal blood vessels are rich with ACE-2 receptors.[11] During the infection phase , COVID-19 virus uses the enzymatic receptor of ACE2 to penetrate the host cell , binding of coronavirus with ACE2 leads to down regulation of ACE2 , the result is elevation of angiotensin II level which is accompanied by higher levels of aldosterone and lower levels of potassium.[20] This complicated biochemical relationship between ACE2 and potassium lower levels highlights Pfizer Biontech role. Regarding AstraZeneca Oxford vaccine, L-histidine and L-histidine hydrochloride monohydrate are essential biochemical components within the vaccine chemical structure.[21] Histidine is an essential amino acid in mammals,[22] histidine is converted to histamine by histidine decarboxylase,[23] also it can pass irreversible degradation.[22] Hence , histidine is a component of solutions used in cardiac surgery for oxygen preservation and also has a role against inflammatory bowel disease. [23] It has a specific role on astrocytes by protecting them from oxygen-glucose deprivation.[22] Remarkably, histidine is responsible for iron binding in hemoglobin and myoglobin.[23] Additionally histidine-rich glycoprotein plays a key role in regulation coagulation process by interacting with a number of ligands including fibrinogen , heparin and also regulating the immune system by interacting with several ligands such as phospholipids (which protect the cell as a barrier) and zinc[23,24] which modulate the inflammatory responses.[25] Moreover, most histamine (resulting from histidine decarboxylation) is synthesized and stored in immune cells (mast calls

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and basophils) because histamine receptors (H4) are expressed within those cells.[23] On the other hand, magnesium chloride hexahydrate is a biochemical compound within AstraZeneca Oxford vaccine structure.[21] Similarly , magnesium chloride improves immune system function [26] and reduces blood coagulation by binding with coagulation factors IX and X.[27] Taken histidine and magnesium chloride together , AstraZeneca Oxford has a great role in supporting the immune system , regulating blood coagulation and inflammatory responses on the basis of its biochemical ingredients . This is why D- dimer level was highly significantly decreased and CRP was significantly decreased in Ga_1 and Ga_2 compared with Gc. Definitely, the non-significant difference between Ga_1, Ga_2, and Gh for both D-dimer and CRP indicates the reactive role of AstraZeneca Oxford vaccine in shifting D-dimer and CRP towards the balance. Interestingly, the present study is the first to highlight the great role of AstraZeneca Oxford vaccine in Iraqi patients on the basis of its chemical structure. Aluminum hydroxide constitutes the adjuvant material within Sinopharm vaccine.[28] Generally, aluminum salts have been used as vaccines adjuvants for more than half century , they are recently found in at least 146 globally licensed vaccines due to the aluminum salt property that an antigen absorbed to it may result in improved immune potency of aluminum absorbed antigen.[29] In this regard , a recent study has reported that administration of aluminium hydrogen nanoparticles promotes the cellular immune response and could be applied to designing new vaccines against tuberculosis.[30] Another recent study has indicated that aluminum hydroxide is widely used as adjuvant in human vaccines caused by it enhances the activation of antigen processing and presentation pathways (in vitro) . Moreover , intramuscular immunization with aluminum hydroxide could attract neutrophils to the site of injection and regulate various immune system related processes.[31] Additionally , aluminum salt/ antigen binding within the vaccine structure promotes antigen uptake and presentation by antigen –presenting cells.[32] This is why CRP level was significantly decreased in sera of Gs_1 and Gs_2 compared with Gc , table 3. Remarkably, the significant decrease of CRP level in Gs1 compared with Gh and the non-significant difference between Gs2 and Gh reflect the reactive role of Sinopharm vaccine in modulating CRP level towards balance. In contrast, as mentioned in table 2 D-dimer level was none significantly decreased in Gs_1 compared with Gc and a highly significant increase in Gs2 compared with Gc. These controversial results are explained as side effects of aluminum hydroxides, a previous study has reported that aluminium hydroxide acts as coagulants. [33] Another previous study has revealed that aluminium derivatives in general functions as coagulants.[34] The significant and highly significant increase of D-dimer level in Gs1 and Gs2 respectively compared with Gh indicates the side effect of Sinopharm vaccine regarding coagulation. Remarkably , D-dimer level is so high in Gs_2 compared with Gh , table 2, this is reflected by the two doses of the vaccines (high level of aluminum derivatives functioned as coagulants).[28] Lastly, regarding immunoglobulin levels (COVID-19 IgG and COVID-19 IgM) in Gp1 , Gp_2 , Ga_1 , Ga_2 , Gs_1 and Gs_2 in table 4 and table 5 respectively , the high prevalence of COVID-19 IgG and COVID-19 IgM after taking Pfizer Biontech vaccines agrees with the recent study[1] that indicated vaccines support the immune system to fight pathogens by releasing specific immune responses.[35] Indeed, infected people with COVID-19 patients characterized by higher levels of COVID-19 IgG and COVID-19 IgM.[36] Remarkably, IgG is so high in Ga_2 , table 4 , this is mostly reflected by the potential role of the two doses of the vaccine on astrocytes which protecting from oxygen-glucose deprivation. Also, results of table 5 have revealed a gap of IgM in the vaccination of Gp_2 compared with Gp_1 and clearly Gp_2 is so high compared with Gc. Since potassium derivatives are the basic components of Pfizer biontech vaccine,[16] a previous study has revealed that IgM suppress voltage gated potassium channels in acquired neuromyotonia (autoimmune disorder specific with potassium).[37]

Although a wide range of studies dealt with COVID-19 disease since 2020 the present study is the first submitting novel findings related to the three vaccines taken in Iraq on the basis of chemical aspects. The present study significantly presents novelty to chemistry generally and biochemistry specifically regarding COVID-19. Interestingly, the present study is the first providing insights into the pivotal role of Pfizer biontech vaccine in Iraqi

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COVID-19 patients by shifting D-dimer towards balance and depressing the level of CRP (a major biochemical marker of inflammation) in the term of potassium derivatives which constitutes the major chemical component of this vaccines. Also, the present study is the first highlighting the pivotal role of AstraZeneca Oxford vaccine in Iraqi COVID-19 patients by shifting D-dimer and CRP towards balance in the term of its chemical structure containing L-histidine and magnesium chloride. Moreover, the present study is the first highlighting the reactive biochemical action of Sinopharm vaccine in Iraqi COVID-19 patients by shifting CRP towards balance in the term of aluminum hydroxide which constitutes the most important compounds within the vaccine structure. Sinopharm action on D-dimer for patients who receive the first dose of the vaccine was reasonable but was controversial for patients who receive the two doses due to the side effect of aluminum hydroxide as a coagulant. Finally, the present study has revealed a complicated biochemical relationship between ACE2 and lower levels of potassium, which provided insights into the importance of potassium derivatives within Pfizer Biontech structure.

Table 2. D-dimer levels (ng/mL) in sera of the studied groups

Group	D-dimer (ng/mL) Mean±SEM	P value
Gh	282±5.40	
Gc	865.2±11.05	**pGc/Gh: H.S ($6.23E^{-05}$)**
Gp_1	338.5±9.1	**pGp_1/Gc: H.S(0.00015)**
		pGp_1/Gh: N.S (0.373)
Gp_2	432.6±19.8	**pGp_2/Gc: S(0.05)**
		pGp_2/Gh: N.S (0.119)
Ga_1	290.4±2.3	**pGa_1/Gc: H.S (5.22E-05)**
		pGa_1/Gh:N.S (0.802)
Ga_2	348.8±103.1	**pGa_2/Gc: H.S (0.000877)**
		pGa_2/Gh:N.S (0.188)
Gs_1	568.7±25.5	**pGs_1/Gc: N.S(0.079)**
		pGs_1/Gh: S (0.0328)
Gs_2	2107.6±1192.9	**pGs_2/Gc: H.S(0.001)**
		pGs_2/Gh:H.S (0.0003)

Table 3. CRP levels (mg/dL) in sera of the studied groups

Group	CRP mg/dL Mean±SEM	P value
Gh	4.80±1.22	
Gc	59.07±5.80	**pGc/Gh: S(0.0018)**
Gp_1	7.15±1.71	**pGp_1/Gc: S (0.002)**
		pGp_1/Gh: N.S (0.1869)
Gp_2	7.96±0.68	**pGp_2/Gc: S (0.0012)**
		pGp_2/Gh: S (0.00595)
Ga_1	5.46±2.42	**pGa_1/Gc: S(0.002)**
		pGa_1/Gh:N.S (0.590)
Ga_2	5.44±1.75	**pGa_2/Gc: S (0.0051)**
		pGa_2/Gh: N.S (0.59)
Gs_1	2.45±1.31	**pGs_1/Gc: S (0.0013)**
		pGs_1/Gh: S (0.0289)
Gs_2	5.39±1.92	**pGs_2/Gc: S (0.0055)**
		pGs_2/Gh: N.S (0.630)

Table 4. COVID-19 IgG levels (mLU/mL) in sera of the studied groups.

Group	COVID-19 IgG (mLU/mL) Mean±SEM	P value
Gh	0.43±0.28	
Gc	6.72±2.18	**pGc/Gh: S (0.004)**

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Gp_1	5.04±0.85	**pGp_1/Gc: N.S (0.366)** **pGp_1/Gh: H.S ($5.51E^{-7}$)**
Gp_2	5.20±0.70	**pGp_2/Gc: N.S (0.405)** **pGp_2/Gh: H.S ($2.12E^{-08}$)**
Ga_1	6.11±0.83	**pGa_1/Gc: N.S (0.762)** **pGa_1/Gh: H.S ($1.6E^{-07}$)**
Ga_2	22.00±1.60	**pGa_2/Gc: H.S (0.0002)** **pGa_2/Gh: H.S ($2.54E^{-07}$)**
Gs_1	4.81±1.12	**pGs_1/Gc: N.S (0.3631)** **pGs_1/Gh: H.S ($4.34E^{-05}$)**
Gs_2	1.86±0.62	**pGs_2/Gc: S (0.040)** **pGs_2/Gh: S (0.00016)**

Table 5. COVID-19 IgM levels (mLU/mL) in sera of the studied groups.

Group	COVID-19 IgM (mLU/mL) Mean±SEM	P value
Gh	0.55±0.28	
Gc	1.48±0.47	**pGc/Gh: H.S ($2.35E^{-4}$)**
Gp_1	0.553±0.462	**pGp_1/Gc: H.S ($2.4E^{-4}$)** **pGp_1/Gh: N.S (0.979)**
Gp_2	2.97±0.27	**pGp_2/Gc: H.S ($2.56E^{-06}$)** **pGp_2/Gh: H.S ($2.73E^{-12}$)**
Ga_1	1.36±0.65	**pGa_1/Gc: N.S (0.707)** **pGa_1/Gh: S (0.006)**
Ga_2	1.15±0.08	**pGa_2/Gc: N.S (0.358)** **pGa_2/Gh: S (0.047)**
Gs_1	1.09±0.39	**pGs_1/Gc: N.S (0.111)** **pGs_1/Gh: S (0.003)**
Gs_2	1.33±1.70	**pGs_2/Gc: N.S (0.501)** **pGs_2/Gh: S (0.007)**

Conclusion

- The present study submits a novelty to the field of COVID-19 by highlighting the chemical aspect of vaccine structures used in Iraq and gives new findings to chemistry generally and biochemistry specifically regarding COVID-19.
- The present study is the first providing insights into the pivotal biochemical role of Pfizer Biontech vaccine in Iraqi COVID-19 patients by shifting the D-dimer level (a major biochemical marker of coagulation) towards the balance and decreasing CRP level (a major biochemical marker of inflammation) in the term of potassium derivatives which constitute a major chemical components within the vaccine structure.
- The present study is the first highlighting the great biochemical role of AstraZeneca Oxford vaccine in Iraqi COVID- 19 patients by shifting D-dimer and CRP levels towards the balance in the term of L-histidine and magnesium chloride which constitute major chemical components within the vaccine structure.
- The present study is the first highlighting the reactive biochemical action of Sinopharm vaccine in Iraqi COVID-19 patients by shifting CRP level towards the balance in the term of aluminum hydroxide which constitutes a crucial chemical component within the vaccine structure.
- Sinopharm action on D-dimer for patients who received the first dose of the vaccine was reasonable but was controversial for those who received the two doses due to the side effect of aluminum hydroxide as a coagulant.
- Despite the three vaccines mentioned above minimizing the inflammation severity but not preventing the infection to have occurred, this is reflected and indicated by the high prevalence of COVID-19 IgG and IgM in vaccinated

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patients which released to support the immune system.

- The complicated biochemical relationship between ACE2 and the lower levels of potassium in COVID-19 patients provided insights for the importance of potassium derivatives within Pfizer Biontech structure.

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Authors' Declaration

- Conflicts of Interest: None.
- I hereby confirm that all the Figures and Tables in the manuscript are mine. Furthermore, any Figures and images, that are not mine, have been included with the necessary permission for re-publication, which is attached to the manuscript.
- Authors sign on ethical consideration's approval.
- Ethical Clearance: the project was approved by the ethical committee in The International Center for research and Development (ICRD) in Baghdad / Al Atayfya. Also the project was approved by University of Baghdad.

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دراسة بعض المتغيرات الكيموحيوية لمرضى عراقيين مصابين بكورونا 19

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الخلاصة

تهدف الدراسة الحالية الى مقارنة التأثير الكيموحيوي للقاحات الثلاثة المعطاة في العراق و هي : فايزر بايونتيك ، أسترازينيكا أوكسفورد و السينوفارم و بالإعتماد على متغيرات كيموحيوية. تم إشتراك سبعون عراقيا مصابا بكوفيد 19 (ذكور و إناث) و تم تصنيفهم إلى سبعة مجاميع : المجموعة c تتضمن مصابين بكوفيد 19 (بدون لقاح) ، المجموعة p1 تتضمن مصابين بكوفيد 19 بجرعة واحدة من فايزر بايونتيك ، المجموعة p2 تتضمن مصابين بكوفيد 19 بجرعتين من فايزر بايونتيك ، المجموعة a1 تتضمن مصابين بكوفيد 19 بجرعة من أسترازينيكا أوكسفورد ، المجموعة a2 تتضمن مصابين بكوفيد 19 بجرعتين من أسترازينيكا أوكسفورد ، المجموعة s1 تتضمن مصابين بكوفيد 19 بجرعة من السينوفارم و المجموعة s2 تتضمن مصابين بكوفيد 19 بجرعتين من السينوفارم . تم مقارنة المرضى مع اصحاء (بدون لقاح) كمجموعة ضابطة. أشارت النتائج إلى أن مستوى د-دايمر ارتفع بشكل معنوي عالي في c مقارنة مع h بينما إنخفض بشكل معنوي عالي في p1 ، a1 ، a2 و معنويا في p1 و غير معنوي في s1 و إرتفع بشكل معنوي عالي في s2 مقارنة مع c . إن مستوى البروتين الفعال سي إرتفع بشكل معنويا في c مقارنة مع h بينما إنخفض معنويا في p1، p2، a1 ، a2 ، s1 ، s2 مقارنة مع c إن مستوى الإمينوغلوبيولين ج مستوى الإميونوغلوبيولين م إرتفعت في c بينما إنخفضت بعد أخذ اللقاح بإستثناء a2 بما يخص الإمينوغلوبيولين ج و p2 بما يخص الإميونوغلوبيولين م. الدراسة الحالية قدمت حداثة إلى مجال كوفيد19 بتسليطها الضوء على الجوانب الكيميائية للقاحات المستعملة في العراق .

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