

Study of ATP/GTP binding protein -1 (AGTPBP-1) in Fibrotic Lung Disease with and without COVID-19 Vaccination

Raed Mahmoud Al-Azawee ^{*,1}  and Zeinab M. Al-Rubaei  ¹

¹ Department of Chemistry, College of Education for Pure Science (Ibn Al-Haitham), University of Baghdad, Baghdad, Iraq.

*Corresponding author

Received 17/12/2023, Accepted 2/5/2024, Published 20/9/2025



This work is licensed under a Creative Commons Attribution 4.0 International License.

Abstract

It took less than two months for the severe acute respiratory syndrome that caused by coronavirus disease 2019 to become a pandemic. ATP/GTP binding protein -1 (AGTPBP-1) is responsible for encoding a number of proteins, including cytosolic carboxypeptidase1 (CCP1), which has been investigated in degenerative diseases also has a role in the regulation of polyglutamylation of tubulin. Patients and methods: A 150 people participated in this study were split into three groups, The first group (G₁), served as control group included (50) subjects. Second group (G₂) consisted of (50) Fibrotic Lung Disease (FLD) patients without COVID-19 vaccine. Third group (G₃) consisted of (50) FLD patients with COVID-19 vaccine. Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP), Lactate Dehydrogenase (LDH), Ferritin D-dimer. were measured by enzymatic method. AGTPBP1 levels were measured using the ELISA technique. Results: show highly significant increases in ESR, CRP and LDH levels among three groups. ANOVA descriptive analysis of Ferritin, D-dimers and AGTPBP1 for all studied groups. Show a significant increase in levels of G₃ and G₂ comparing to G₁. In addition, a significant increase found in G₃ comparing to G₂. The present study submits novelty in COVID-19 fields by Focus on role of new parameter such as AGTPBP-1 in corona-19 vaccine (Pfizer) that used in Iraq.

Keywords: ATP/ GTP Binding Protein, COVID-19 Vaccination ,CRP, D-dimer, Fibrotic Lung.

Introduction

Patients with FLD, a severe respiratory ailment, are predicted to have respiratory failure also eventually perish away as a result of increased lung scarring within three to five years of receiving a diagnosis of the condition ⁽¹⁾.The pandemic of coronavirus disease 2019 which is caused by the severe acute respiratory illness caused by coronavirus-2, has had an effect on almost every aspect of patient care. Patients that infection with coronavirus may be influenced with FLD in a variety of way that consider the similar risk factors for negative outcomes between these two patient populations ⁽²⁾.

The AGTPBP-1protein known as cytosolic carboxypeptidase 1 (CCP1), that helps enable deglutamylation, which is necessary for maintaining steady-state levels of polyglutamylated tubulin ⁽³⁾.When compared to the expression of AGTPBP-1 in other tissues, the level of expression in normal lung tissue is somewhat higher. The process of deglutamylation of tubulin is mediated by CCP1, which is encoded by AGTPBP1. This process may have an effect on the microtubule network as well as

the dynamics of tubulin in lung cancer ⁽⁴⁾. The researchers used short-hairpin RNA (shRNA) to silence lung cancer cells and examine their impact on migration, proliferation, and cancer stemness. The predictive significant of AGTPBP-1 and its related pathways in lung cancer was studied using an assessment of publicly available lung cancer datasets. Indirect indicators of thrombotic activity, D-dimer, which is a fibrin breakdown product, are widely established in the context of assessing the risk of developing venous thromboembolism in the general population ^(5,6).

The D-dimer test is a sensitive diagnostic tool that is used in clinical practise to identify thrombotic diseases including pulmonary embolism. D-dimer increasing in COVID-19 carriers may thus be beneficial in the detection of individuals who have advanced lung difficulties and thromboembolism ⁽⁷⁾. Aim of study: Aim of the present study was to determine CRP, D-dimer and AGTPBP-1 in FLD patients with and without COVID-19 vaccine and compare results with the control group. In addition ROC study were tested for AGTPBP-1, that may be considered an important prognostic factor in COVID-19 vaccine.

Materials and Methods

In January 2022 to March 2023, respectively, personnel from the Baquba also Ibn Al-Nafis teaching hospitals provided their services to collect samples for the purpose of this inquiry. Thus, there were a total of three groups comprising 150 participants. The first group (G₁), which served as the control group, was comprised of fifty different volunteers. None of the fifty patients with FLD who were assigned to the second group (G₂) had been vaccinated against COVID-19. Fifty FLD patients who had previously been vaccinated against COVID-19 made up the participants in the third group (G₃). The ages of all of the participants ranged anywhere from 25 to 55 years old. Every patient was interviewed in person utilizing a specially crafted questionnaire that contained a comprehensive medical history also a variety of probing questions. A sample of five millilitres of venous blood was collected from each person. The D-dimer also AGTPBP-1 levels in the serum were measured utilizing the ELISA technique utilizing kits purchased from My Bio Source in the United States. The ESR, CRP, LDH, also ferritin levels in the serum were all tested manually.

Results and Discussion

This is the first research that, to the best of our knowledge, has discovered AGTPBP -1 in

fibrosis lung illness, also it was done both with also without the COVID-19 vaccination. Participants in the present research ranged in age from 25 to 55 that were divided into three groups. The G₁ consisted of the control group (N= 50) participants. Patients who were assigned to the G₂ (with a total of 50 patients) were not given the COVID-19 vaccine. People who in the G₃ had lung fibrosis with receiving COVID-19 vaccine. It is imperative that a thorough computed tomography (CT) scan be performed. According to the research that was conducted in the past, this examination need to consist of both an expiratory thin-section CT scan also a helical supine inspiratory chest CT scan capture with contiguous or overlapping thin section reconstructions of 1.5 millimetres. After infection with COVID-19, several individuals were found to have cysts, mosaic attenuation, also newly developed emphysema, all of which lend credence to the hypothesis that the virus is occasionally the cause of airflow limitation^(8,9).

Table (1) displays ESR, CRP, and LDH levels in G₁G₂ and G₃. Results show a highly significant increases in ESR, CRP and LDH levels among three groups. Results are in agreement with many researches revealed that ESR, CRP and LDH as a valuable predictor and critical measure of COVID-19 progression and severity^(10,11).

Table 1. ANOVA Descriptive Analysis of ESR, CRP and LDH levels in patients and control groups.

Groups	G ₁	G ₂	G ₃	P-value
ESR mm/hr.	10.21 ± 2.29	32.93 ± 9.32	93.09 ± 20.21	HS
CRP mg /L	6.12 ± 1.93	50.31 ± 10.98	95.44 ± 20.25	HS
LDH U/L	150.34 ± 22.55	490.32 ± 50.59	760.53 ± 80.01	HS

HS: High Significantly correlation between parameters (p value ≤ 0.01).

The majority of COVID-19 infections in children only manifest themselves with modest clinical symptoms also do not cause an increase in CRP or any other biomarker values. On the other halso, the amount of COVID-19 that is found in adults has been shown to have a positive correlation with ferritin, CRP, also ESR levels during the course of this research⁽¹²⁾.

The hypothesis proposed that the early commencement of inflammation would be driven by the release of proinflammatory parameters, which have been demonstrated to be higher in COVID-19. In addition, inflammation-induced cellular damage may cause ferritin to seep out of cells also into the bloodstream, which may cause blood ferritin levels to rise⁽¹³⁾. The severity of COVID-19 has been demonstrated to be connected with high LDH levels, which often suggest tissue damage, according to a number of local studies that have been conducted recently⁽¹⁴⁾. According to the findings of our

research, elevated levels of LDH in individuals with early stages of COVID-19 may suggest a preclinical tissue damage. Despite the fact that the virus attaches to the angiotensin-converting enzyme 2 (ACE2) receptor found in the lungs^(15,16). Lungs are one of the organs that are affected the earliest on in the disease. On the other hand, when the sickness progresses to a severe stage, patients may have multiple organ failure in addition to other parameters abnormalities that indicate to organ damage caused by the over activity of the immune system. Han et al. arrived at the conclusion that either there is a substantial cooperation between lung damage also the severity of the sickness or because COVID-19 directly destroys the target organ, caulitizing the death of the liver heart muscle, rather than hypoxia that is brought on by lung injury⁽¹⁷⁾. The descriptive results of the ANOVAs performed on ferritin, D-dimers, also AGTPBP-1 are shown in Table (2) for each of the groups that

were investigated. The findings showed that G₃ also G₂ had significant greater levels of ferritin also D-dimers compared to G₁, which had the lowest levels.

In addition, in comparison to G₂, G₃ shown a significant increase in growth .

Table 2. ANOVA Descriptive Analysis of Ferritin, D-dimer and ATP/ GTP binding protein in patients and control groups.

Groups	G ₁	G ₂	G ₃	P-value
Ferritin ng/mL	80.52± 10.92	190.85±30.99	280±90.01	S
D-dimers mg/L	0.539±0.142	98.67±18.23	220.1± 38.29	S
AGTPBP1ng/mL	2.52±0.29	6.98±0.35	8.99±1.21	HS

S: Significantly correlation between parameters (0.01 < p value ≤ 0.05).

HS: High Significantly correlation between parameters (p value ≤ 0.01).

In addition, AGTPBP-1 levels were shown in Table (2), which revealed a statistically significant increase in G₃ also G₂ in comparison to G₁. Additionally, there was a very significant increase found G₃comparing to G₂ in terms of magnitude . A recent research found that those who were diagnosed with severe COVID-19 had considerably greater levels of AGTPBP-1, D-dimer, also ferritin than those who were diagnosed with less severe instances. This result was in agreement with the findings of previous publications^(18, 19). According to the findings of the research, having an increased D-dimer level may be an indicator of the severity of the illness, as well as potential lung also thromboembolic events⁽²⁰⁾ . In response to infections, the liver produces copious amounts of a protein known as CRP that is seen in the acute phase of the immune response. This protein is a very sensitive sign of the presence of infection as well as damage to the tissue. There have been a number of studies that have shown a correlation between CRP levels and COVID-19 severity, also these studies imply that this correlation might be utilised as a stalsoleone risk factor to predict the severity of the illness⁽²¹⁾.

There was a significant inverse cooperation between COVID-19 severity with levels of ferritin, LDH, D-dimer, also CRP. Higher levels of these parameters may be used as a predictor for the severity of COVID, according to certain studies^(22, 23).

When severe COVID-19 patients were compared to non-severe cases, the inflammatory markers ESR, CRP, ferritin, also D-dimer showed higher medians in the severe group disease. It is recommended that these signs be employed in the prompt detection of severe sickness in corona virus

patients in order to allow the early starting of effective medication. This will make it possible to begin treatment earlier^(24,25).

Examine the biochemical activity of the Pfizer vaccine in Iraqi corona virus patients by altering the amounts of D-dimer also CRP back into balance⁽²⁶⁾ .Authors proposed utilizing larger research samples also a new research design on a broader age range in order to confirm the results of the COVID-19 vaccine⁽²⁷⁾.The AGPBP-1 expression was shown to have a positive link with overall patient survival in lung cancer, with the expression of AGPBP-1 being lower in cancer tissues than in normal counterparts. The expression of ATPBP-1 also immune infiltration were both shown to be linked with lung cancer. As a consequence of this, researchers were able to determine the role that AGTPBP1 plays in lung cancer also its significant as a survivor predictor⁽²⁸⁾.

Receiver operating characteristic study for AGTPBP-1

The Receiver Operating Characteristic (ROC) curve analysis for AGPBP-1 across three distinct groups reveals an impressive area under the curve (AUC) value of 0.91. This AUC value is statistically significant at a confidence level of 95%, as indicated by the p-value of 0.0001, which is less than the threshold of 0.01.

The optimal cut-off value for AGTPBP-1 is determined to be 5.18, with a sensitivity of 93% and a specificity of 90%. This suggests a high level of accuracy in distinguishing between the patients groups. These findings are graphically represented in Table (3) and " Figure.1", which visually illustrates the robustness and efficacy of the AGTPBP-1 test across the groups.

Table 3. Difference between sensitivity and specificity of AGTPBP-1.

Variables	Sensitivity	Specificity	Area under the curve	95% C.I.		Cut off value	
				L.B.	U.B.		
AGTPBP-1	0.93	0.90	0.91	0.84	0.98	5.18	

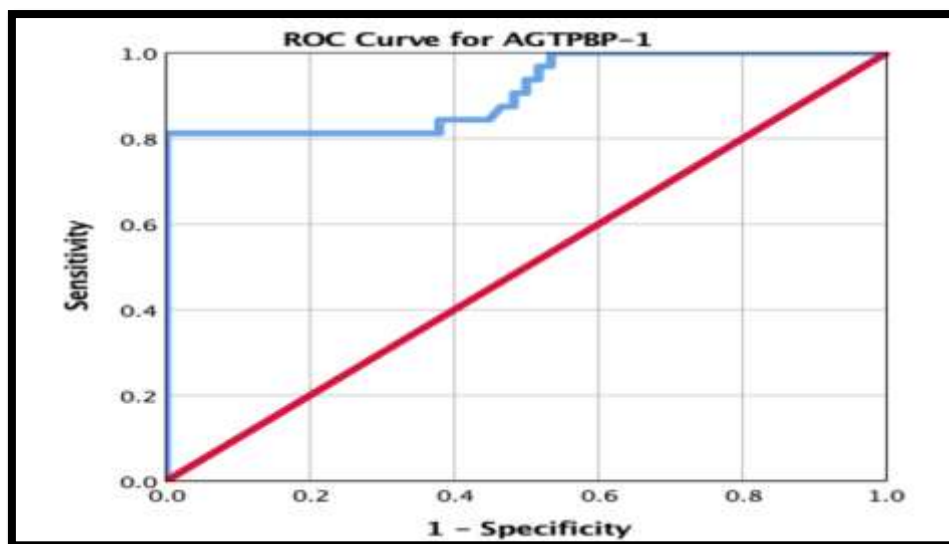


Figure .1 ROC curve of AGTPBP-1

Conclusion

The results showed that highly increase in AGTPBP1 levels to lung Fibrotic patients with vaccination comparing to lung fibrotic without Vaccine and contact may be helpful in the identification of lung fibrotic development in this group and may be used as a marker to follow up and therapeutic purpose. Farther studies need to improve application of AGTPBP1 in lung fibrotic patients with and without Vaccine. In addition findings of **cu mat study** suggested that serum CRPLDH and D-dimers levels could be used as an essential indicator of the progression and the severity of COVID-19. After completing the study, we extend our thanks , appreciation and gratitude first to the patients without whom this study would not have been completed, and thanks to Dr. Imad Ahmed Latif at the Baquba Teaching Hospital for the great contribution to this research. All appreciation goes to the mother University of Baghdad for providing the necessary supplies for the research.

Conflicts of Interest

The authors declare that there is no conflict of interest.

Funding

The authors received no financial support for the research, authorship and /or publication of this article.

Ethics Statements

The ethical principles outlined in the Helsinki Declaration were adhered to throughout the course of the research that was conducted. The patient's verbal also written agreement for the analysis was acquired before obtaining a sample from them. Document number 54 (which contains the number also date in 5 March 2023) was reviewed by a community ethics committee, also it was determined that the research protocol, subject

information, also consent form were all acceptable for use in the research.

Author Contribution

Raed Mahmoud Al-Azawee , Zeinab M. Al-Rubaei contributed to the design and implementation of the results and to the writing of the manuscript.

References

1. Glass DS, Grossfeld D, Renna HA, Agarwala P, Spiegler P, DeLeon J, Reiss AB. Idiopathic pulmonary fibrosis: Current and future treatment. *Clin Respir J*. 2022;16(2):84-96.
2. Wong AW, Fidler L, Marcoux V, Johansson KA, Assayag D, Fisher JH, Hambly N, Kolb M, Morisset J, Shapera S, Ryerson CJ. Practical considerations for the diagnosis and treatment of fibrotic interstitial lung disease during the coronavirus disease 2019 pandemic. *Chest*. 2020;158(3):1069-1078.
3. Rogowski K, Van Dijk J, Magiera MM, Bosc C, Deloulme JC, Bosson A, Peris L, Gold ND, Lacroix B, Grau MB, Bec N. A family of protein-deglutamylating enzymes associated with neurodegeneration. *Cell*. 2010; 12;143(4):564-578.
4. Parker AL, Kavallaris M, McCarroll JA. Microtubules and their role in cellular stress in cancer. *Front Oncol*. 2014 ; 18;4:153.
5. Weitz JI, Fredenburgh JC, Eikelboom JW. A test in context: D-dimer. *JACC*. 2017;70(19):2411-20.
6. Facciorusso A, Del Prete V, Antonino M, Neve V, Crucinio N, Di Leo A, Carr BI, Barone M. Serum ferritin as a new prognostic factor in hepatocellular carcinoma patients treated with radiofrequency ablation. *J Gastroenterol Hepatol*. 2014;29(11):1905-1910.
7. Lippi G, Favaloro EJ. D-dimer is associated with severity of coronavirus disease 2019: a pooled

- analysis. *Thromb Haemost.* 2020;120(05):876-888.
8. Nagpal P, Guo J, Shin KM, Lim JK, Kim KB, Comellas AP, Kaczka DW, Peterson S, Lee CH, Hoffman EA. Quantitative CT imaging and advanced visualization methods: potential application in novel coronavirus disease 2019 (COVID-19) pneumonia. *BJR| Open.* 2021;3(1):20200043.
 9. Al-Mendalawi MD. Two Decades in the Journey of Al-Kindy College Medical Journal: Key Barriers, Achievements, and Prospects. *KCMJ.* 2022;18(1):3-4.
 10. Zyara AM, Aldoori AA, Samawi FT, Kadhim SI, Ali ZA. A relationship study of coronavirus (COVID-19) infection, blood groups, and some related factors in Iraqi patients. *Baghdad Sci. J.* 2023;20(4 (SI)):1459-1468.
 11. Ismael MK, Aldabagh MA, Rasuol LM. Matrix Metalloproteinase-3 and Tissue inhibitor of metalloproteinase-2 as Diagnostic Markers for COVID-19 Infection. *IJS.* 2022 Sep 30:3679-3687.
 12. Buti, R. H., El-Yassin, H. D., & Alwan, N. A. S. A. Evaluation of CRP, D-Dimer of clinical significance in Iraqi patients with COVID-19 and associated comorbidities. *IJHS.* 2022; 6(S8): 1505–1513.
 13. Lin Z, Long F, Yang Y, Chen X, Xu L, Yang M. Serum ferritin as an independent risk factor for severity in COVID-19 patients. *Journal of infection.* 2020;81(4):647-679.
 14. Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J, Fan Y, Zheng C. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. *Lancet Infect Dis.* 2020;20(4):425-434.
 15. Shi J, Li Y, Zhou X, Zhang Q, Ye X, Wu Z, Jiang X, Yu H, Shao L, Ai JW, Zhang H. Lactate dehydrogenase and susceptibility to deterioration of mild COVID-19 patients: a multicenter nested case-control study. *BMC Med.* 2020;18:1-6.
 16. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, Si HR, Zhu Y, Li B, Huang CL, Chen HD. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature.* 2020 ;579(7798):270-3.
 17. Han Y, Zhang H, Mu S, Wei W, Jin C, Tong C, Song Z, Zha Y, Xue Y, Gu G. Lactate dehydrogenase, an independent risk factor of severe COVID-19 patients: a retrospective and observational study. *Aging (Albany NY).* 2020;12(12):11245.
 18. Feng Y, Ling Y, Bai T, Xie Y, Huang J, Li J, Xiong W, Yang D, Chen R, Lu F, Lu Y. COVID-19 with different severities: a multicenter study of clinical features. *Am J Respir Crit Care Med.* 2020;201(11):1380-1388.
 19. Wu C, Chen X, Cai Y, Zhou X, Xu S, Huang H, Zhang L, Zhou X, Du C, Zhang Y, Song J. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. *JAMA Intern Med.* 2020;180(7):934-943.
 20. Düz ME, Balcı A, Menekşe E. D-dimer levels and COVID-19 severity: Systematic Review and Meta-Analysis. *Tuberk Toraks.* 2020 Dec;68(4):353-360.
 21. Liu F, Li L, Xu M, Wu J, Luo D, Zhu Y, Li B, Song X, Zhou X. Prognostic value of interleukin-6, C-reactive protein, and procalcitonin in patients with COVID-19. *J Clin Virol.* 2020;127:104370.
 22. Mohammed SK, Taha MM, Taha EM, Mohammad MN. Cluster analysis of biochemical markers as predictor of COVID-19 severity. *Baghdad Sci. J.* 2022;19(6 (Supl.)):1423-1429.
 23. Al-Mendalawi MD. The Scientific Contribution of the Al-Kindy College Medical Journal to the World Literature on the COVID-19 Pandemic. *KCMJ.* 2023;19(1):1-2.
 24. Al-Humairi RM, Muhsin HY, Ad'hiah AH. Severity of Coronavirus Disease 19: A Profile of Inflammatory Markers in Iraqi Patients. *MJMHS.* 2022;18(1).
 25. Al-Mamoori HS, Ahmed MH, Al-Nafie TY, Al-Attar Z. Assessment of the Level of Protein C in Hospitalized Iraqi Patients with COVID-19 and its Correlation with Hematological and Inflammatory Markers. *Open Access Maced J Med Sci.* 2022;10(A):817-823.
 26. Jasim RZ. Biochemical Action of Vaccines in Iraqi Patients with COVID-19 Infection. *Baghdad Sci. J.* 2023;20(4 (SI)):1469-1479.
 27. Hamid MK. Impact of COVID-19 Vaccine on Hearing Status of Young Ages (Medical College Students as a Sample). *Baghdad Sci. J.* 2023;20(4 (SI)):1498-1506.
 28. Kwak HJ, Gil M, Chae HS, Seok J, Soundrarajan N, Saha SK, Kim A, Park KS, Park C, Cho SG. Expression of ATP/GTP Binding Protein 1 Has Prognostic Value for the Clinical Outcomes in Non-Small Cell Lung Carcinoma. *J Pers Med.* 2020;10(4):263.

دراسة البروتين الرابط للنيوكليوتيدات في مرض التليف الرئوي للملقحين وغير الملقحين لفايروس كورونا

رائد محمود العزاوي^١ و زينب منيب الربيعي^٢

^١ قسم الكيمياء، كلية التربية للعلوم الصرفة (ابن الهيثم)، جامعة بغداد، العراق.

^٢ قسم الكيمياء، كلية التربية للعلوم الصرفة (ابن الهيثم)، جامعة بغداد، العراق.

الخلاصة

استغرق الأمر أقل من شهرين حتى تصبح المتلازمة التنفسية الحادة التي يسببها مرض فيروس كورونا ٢٠١٩ مرض شلل نصفي. البروتين الرابط للنيوكليوتيدات هو بروتين مسؤول عن التشفير العديد من الدلائل، بما في ذلك كاربوكسي ببتيداز الخلوي، والذي تم بحثه في الأمراض التنكسية وله أيضاً دور في تنظيم تعدد الجلوتامين للتبولين. المرضى وطرق العمل: شارك في هذه الدراسة ١٥٠ شخصاً تم تقسيمهم إلى ثلاث مجموعات، المجموعة الأولى (G₁)، كانت بمثابة مجموعة ضابطة وتضمنت (٥٠) شخصاً. المجموعة الثانية (G₂) تكونت من (٥٠) مريضاً بمرض التليف الرئوي غير الحاصلين على لقاح كوفيد-١٩. المجموعة الثالثة (G₃) تكونت من (٥٠) مريضاً بالتليف الرئوي مع لقاح (فايزر) كوفيد-١٩. تم قياس معدل ترسيب كريات الدم الحمراء (ESR)، البروتين المتفاعل سي (CRP)، وقياس نازع هيدروجين اللاكتات (LDH)، وقياس مخزون الحديد (ferritin)، دي دايمر (D-dimer). بالطريقة الانزيمية و تم قياس مستويات البروتين الرابط للنيوكليوتيدات باستخدام تقنية الاليزا. النتائج: تم استخدام LSD في تحليل النتائج احصائياً حيث أظهرت النتائج زيادة كبيرة في مستويات ESR، CRP، LDH، Ferritin، D-dimers والبروتين الرابط للنيوكليوتيدات لجميع المجموعات المدروسة. تظهر زيادة ملحوظة في مستويات G₂ و G₃ مقارنة بـ G₁. بالإضافة إلى ذلك، تم العثور على زيادة كبيرة في G₃ مقارنة بـ G₂. الاستنتاج: تقدم هذه الدراسة الحالية حادثة في مجالات كوفيد-١٩ من خلال التركيز على دور المعلومات الجديدة مثل بروتين الرابط للنيوكليوتيدات وعامل نقص الأكسجين في لقاح كورونا-١٩ (فايزر) المستخدم في العراق. الكلمات المفتاحية: البروتين الرابط للنيوكليوتيدات، لقاح (فايزر) كوفيد-١٩، بروتين التفاعل سي، دي دايمر، تليف الرئوي.