

How to Cite:

Bhar, M. A., Khalaf, S. J., & Marbut, M. M. (2022). Determination of the concentration of serum ferritin, D-dimer, CRP and IL-6 in patients who affected with COVID-19. *International Journal of Health Sciences*, 6(S4), 9731–9736.
<https://doi.org/10.53730/ijhs.v6nS4.12050>

Determination of the concentration of serum ferritin, D-dimer, CRP and IL-6 in patients who affected with COVID-19

Mohammed Ahmed Bhar

Department of Biochemistry, College of Medicine, University of Tikrit, Tikrit, Iraq
Corresponding author email: Mohammedbahar232@gmail.com

Salim Jasim Khalaf

Department of Biochemistry, College of Medicine, University of Tikrit, Tikrit, Iraq

Mousa Mahmoud Marbut

Department of Biochemistry, College of Medicine, University of Tikrit, Tikrit, Iraq

Abstract---Background; SARS-CoV-2, the novel corona virus that originated in Wuhan, China in late December is a positive single stranded RNA virus. COVID-19, a disease caused by the SARS-CoV-2 is characterized by symptoms such as fever, sore throat, dry cough, loss of sense of taste and smell etc. The symptoms may range from asymptomatic, mild, moderate, severe and critical. The virus enters through its spike protein (S) to the ACE2 receptors. The aim of the study is to evaluation of ferritin, D-dimer, CRP and IL-6 in patients who affected with COVID-19. Patients and methods; A cross-sectional conducted in many Hospitals in Baghdad. This study conducted between January to June 2022 on patients infected with the Corona virus. A total of sixty subjects were participated in the present study. Thirty patients of both sexes, with different ages and in the severity infection with the Corona virus, divided into two groups. Results; There were significant elevations in the concentration of serum ferritin and D dimer of COVID-19 patients, as compared with control healthy subjects. Also, there is significant elevation in the concentration of serum CRP of patients with COVID-19, as compare with control healthy subjects. Moreover, there is significant elevation in the concentration of serum IL-6 in COVID-19 patients, as compared with control healthy subjects.

Keywords---COVID-19, serum ferritin, CRP, D-Dimer, IL-6, Baghdad.

Introduction

COVID-19 disease is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This infectious disease was previously known as Novel Coronavirus-Infected Pneumonia (NCIP) by the WHO, and the virus was dubbed 2019 novel coronavirus (2019-nCoV) ^(1,2). In December 2019, a COVID-19 outbreak caused by the 2019 new coronavirus (SARS-CoV-2) began in Wuhan, Hubei Province, China, and has since been declared a pandemic. The emerging corona virus is a virus encapsulated with a large genome of unfragmented, single-stranded RNA genome, 32 kbps insensitive [Ksiazek,2003], and is a member of the Corona viridae (CoV) family that causes mostly respiratory disease with a wide spread of a range of clinical severity, ranging from Mild asymptomatic symptoms (fever, cough, shortness of breath, muscle pain, diarrhea, and fatigue) in a great proportion of patients to multi-organ sepsis and severe acute respiratory distress syndrome (ARDS). The key receptor for SARSCoV-2 entry into cells is angiotensin-converting enzyme 2 (ACE2), which is expressed in both liver cells and bile duct cells, and direct binding of SARSCoV-2 to ACE2 receptors in cholangiocytes may result in liver damage due to bile duct cell damage ^(3,4). The aim of the study is to evaluate of serum ferritin, D-Dimer, CRP and IL-6 in patients who affected with Covid19.

Patients and methods

A cross-sectional conducted in Al-Yarmouk Teaching Hospital , Al-Imamain Al-kadumain medical city-Baghdad/Iraq & Dar AL Salam field Hospital – Baghdad /Iraq. The study protocol was approved by the Ethical committee of College of Medicine\ Tikrit University. This study conducted between January to June 2022 on patients infected with the Corona virus. A total of sixty subjects were participated in the present study. Thirty patients of both sexes, with different ages and in the severity infection with the Corona virus, divided into two groups.

- A. The 1st group consist from 30 patients they have covid19, the result of the PCR of patients with was positive.
- B. The 2nd group consist of thirty normal healthy subjects they not infected with Corona virus as control.

Laboratory tests were conducted (CRP, IL-6, ferretin, and D-dimer) for both patients and control healthy non-patients, and they were compared. Their age ranged between 23-70 years old.

- A. Group 1 (COVID-19 only) = 61.6 ± 9.7 years.
- B. Group 2 (Control healthy subjects) = 51.2 ± 9.6 years.

Inclusion Criteria

1. Patient currently infected with COVID-19.
2. Healthy subjects as controls

Exclusions criteria included

Patient with DM, thyroidectomy or who is on treatment of thyroid, patient with parathyroidism disease, patient with autoimmune disease like SLE , Rheumatoid arthritis H, patient with liver , kidney and pancreas problem, health subject but the last infection with covid19 was before sex months only or less.

Results

The age of all subjects was ranged between 23-70 years old. There were no significant differences between control and all patients. Regarding serum ferritin, there is significant elevation in the concentration of serum ferritin of COVID-19 patients (823.5 ± 264 ng/ml), as compared with control healthy subjects, (64.2 ± 13 ng/ml; $p \leq 0.001$), Table 1. Also, there is significant elevation in the concentration of D-Dimer in COVID-19 patients (3.6 ± 1.4), as compared with control healthy subjects, (0.19 ± 0.1 $p \leq 0.001$). As shown in table 1.

Table 1 The mean and standard deviation of s. ferritin and D-dimer in patients and control subjects

Study Group	Ferritin ng/ml	D- Dimer ug/ml
COVID-19 patients	823.5 ± 264	3.6 ± 1.4
Control	64.2 ± 13	0.19 ± 0.1
P value	0.002	0.001

Moreover, in present study, there is significant elevation in the concentration of serum CRP of patients with COVID-19 only, (39.1 ± 10.6), as compare with control healthy subjects, (2.1 ± 0.8 ; $p \leq 0.01$). Also, in the present study, there is significant elevation in the concentration of serum IL-6 in COVID-19 patients, (14.6 ± 3.5), as compared with control healthy subjects, (3.9 ± 0.8 ; $p \leq 0.001$), as shown in table (2).

Table (2) The mean and standard deviation of IL-6 and CRP of patients of COVID-19 and control healthy subjects

Study groups	IL-6 pg/ml	CRP mg/l
COVID-19 patients	14.6 ± 3.5	39.1 ± 10.6
Control	3.9 ± 0.8	2.1 ± 0.8
P value	0.001	0.01

Discussion

In this study, also conducted a ferritin analysis on COVID-19 patients and the results were statistically highly significant when compared to control apparently healthy subjects. Infection-induced inflammation causes hyperferritinemia, which should be used to identify high-risk patients and guide anti-inflammatory therapy. Serum ferritin has been linked to poor recovery in COVID-19 patients, with ferritin levels being greater in those with a damaged lung lesion and these results agree with Zhou et al ⁽⁵⁾.

In a study of 20 COVID-19 patients, researchers discovered that those with severe and very severe COVID-19 had higher serum ferritin levels ⁽⁶⁾. Another study found that ferritin levels have risen on entry to the hospital and during the stay in the hospital in individuals who died from COVID-19. Day after 16 during hospitalization, the median ferritin concentrations in all these patients reached the upper detection limit, indicating that ferritin concentrations continued to rise nonstop ⁽⁷⁾

The present study found, a highly significant elevation in serum D Dimer as compared with control healthy subjects. Dimer in the evaluation of patients with possible venous thromboembolism Overall, dynamical changes of D. Dimer level are positively correlated with the prognosis of COVID-19, and these results agree with Ji HL *et al*, Zhou *et al* ^(8,9) .who discovered in their studies in severe cases of COVID-19, infection-induced coagulopathy and subsequent hyper fibrinolysis. Several studies have looked into whether D. Dimer levels may be used to predict patient outcomes, including one in China that looked at the biological parameters of COVID-19 patients with a median age of 62. The average D-dimer level in the 113 patients who died was 4.6 g/mL, while the D. Dimer levels in the 161 patients who lived were 0.6 g/mL. Despite these findings, research suggests that combining D. Dimer testing with other biomarkers can assist in the treatment of COVID-19 patients ⁽¹⁰⁾

Cytokines are small soluble polypeptides of immunological origin play a critical role in mediating inflammatory processes manufactured by macrophages, lymphocytes, monocyte, dendritic cells, neutrophils, endothelial cells, and fibroblasts. Cytokines are the mean of communication between immune and non-immune cells⁽¹¹⁻¹³⁾. Interleukin-6 (IL-6) is a multifunctional inflammatory cytokine that plays an important role in the response to environmental stress and has been implicated in the pathogenesis of many chronic diseases, ^(14,15). An increase in IL-6 levels has previously been observed in patients with respiratory dysfunction implying a possible shared mechanism of cytokine-mediated lung damage caused by COVID-9 infection. Furthermore, it seems that the highly pathogenic SARS-CoV-2 is associated with rapid virus replication and a tendency to infect the lower respiratory tract, resulting in an elevated response of IL-6-induced severe respiratory distress. Thus, the present study, suggest that serial measurement of circulating IL-6 levels may be important in identifying disease progression among COVID-19-infected patients. Increased CRP levels seen with COVID-19 infection could be due to inflammatory cytokines. Pathogens are attacked by cytokines, but if the system becomes overactive, lung tissue is destroyed. Thus, tissue destruction and cytokine release can induce CRP production. Furthermore, severe cases have been reported to be accompanied by secondary infections (bacterial infections) ¹⁶⁻¹⁸⁾.

C-reactive protein has been done to patients infected with the novel corona virus and lying in the hospitals , and the results shown that a significant elevation in serum CRP in COVID-19 patients as compare with controls. These present study agree with Luo *et al* ⁽¹⁹⁾ who found a tenfold increase in the concentration of C-reactive protein in patients infected with the novel corona virus as compared with healthy.

References

1. Al-Mashhadani HA, Alshujery MK, Khazaal FA, Salman AM, Kadhimi MM, Abbas ZM, et al., editors. Anti-Corrosive Substance as Green Inhibitor for Carbon Steel in Saline and Acidic Media. Journal of Physics: Conference Series; 2021: IOP Publishing.
2. Entedhar RS, Rmaid ZJ, Jabir TH (2020) Changes of salivary interleukine17, Apelin, Omentin and Vaspin levels in normal subjects and diabetic patients with chronic periodontitis, Ann Trop Med & Pub Health; 23:S404. DOI: <http://doi.org/10.36295/ASRO.2020.23118>.
3. Fisher D, Heymann D. Q&A: The novel coronavirus outbreak causing COVID-19. BMC medicine. 2020 Dec;18(1):1-3.
4. Intesar Jasim Mohammed, Entedhar Rifaat Sarhat, Marwa Abdul-Salam Hamied ,Thuraia Rifaat Sarhat .Assessment of salivary Interleukin (IL)-6, IL10, Oxidative Stress, Antioxidant Status, pH, and Flow Rate in Dental Caries Experience patients in Tikrit Province. Sys Rev Pharm 2021;12(1):55-59
5. Ji HL, Zhao R, Matalon S, Matthay MA. Elevated plasmin(ogen) as a common risk factor for COVID-19 susceptibility. Physiological Reviews. 2020;100(3):1065–75.
6. Kadhimi MM, AlMashhadani HA, Hashim RD, Khadom AA, Salih KA, Salman AW. Effect of Sr/Mg co-substitution on corrosion resistance properties of hydroxyapatite coated on Ti-6Al-4V dental alloys. Journal of Physics and Chemistry of Solids. 2022;161:110450.
7. Khidoyatova, M. R., Kayumov, U. K., Inoyatova, F. K., Fozilov, K. G., Khamidullaeva, G. A., & Eshpulatov, A. S. (2022). Clinical status of patients with coronary artery disease post COVID-19. *International Journal of Health & Medical Sciences*, 5(1), 137-144. <https://doi.org/10.21744/ijhms.v5n1.1858>
8. Luo X, Zhou W, Yan X, et al. Prognostic value of C-reactive protein in patients with coronavirus 2019. Clinical Infectious Diseases. 2020 Oct 15;71(16):2174-9.
9. Sakka M, Connors JM, Hékimian G, et al. Association between D-Dimer levels and mortality in patients with coronavirus disease 2019 (COVID-19): a systematic review and pooled analysis. JMV-Journal de Médecine Vasculaire. 2020 Sep 1;45(5):268-74.
10. Sarhat E.R. Acute Myocardial Infarction: Melatonin, Apelin, and Visfatin as Predictors of Disease. Diyala Journal of Medicine. 13(2), 2017; 11-17.
11. Sarhat ER, Abid IM, Kamel NA, Sarhat TR, Abass KS. Changes of serum Interleukin and Chemerin levels in patients with Polycystic Ovary syndrome. J Adv Pharm Educ Res. 2021;11(4):11-4. <https://doi.org/10.51847/XP8rpqX3Jx>
12. Sarhat ER, Siham A. Wadi, Ban I Sedeeq. Thuraia R. Sarhat, Nawar.A. Jasim. Study of histopathological and biochemical effect of Punica granatum L.extract on Streptozotocin- induced diabetes in rabbits. Iraqi Journal of Veterinary Sciences, 2019; 33(1):189-194.
13. Sarhat, E. R.; Zbaar, S. A.; Ahmed, S. E.; Ahmed, T. S.; Sarhat, T. R. Salivary biochemical variables of Liver Function in among Individuals with COVID-19 in Thi-Qar Province.Egyptian Journal of Chemistry ; 2022;65(6):305-310

14. Suryasa, I. W., Rodríguez-Gámez, M., & Koldoris, T. (2021). The COVID-19 pandemic. *International Journal of Health Sciences*, 5(2), vi-ix. <https://doi.org/10.53730/ijhs.v5n2.2937>
15. Ulhaq, Zulvikar Syambani, and Gita Vita Soraya. "Interleukin-6 as a potential biomarker of COVID-19 progression." *Medecine et maladies infectieuses* vol. 50,4 (2020): 382-383.
16. Vasileva D, Badawi A. C-reactive protein as a biomarker of severe H1N1 influenza. *Inflammation Research*. 2019 Jan;68(1):39-46.
17. Zhou B, She J, Wang Y, Ma X. Utility of ferritin, procalcitonin, and C-reactive protein in severe patients with 2019 novel coronavirus disease.2020.
18. Zhou B, She J, Wang Y, Ma X. Utility of ferritin, procalcitonin, and C-reactive protein in severe patients with 2019 novel coronavirus disease.2020
19. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The lancet*. 2020 Mar 28;395(10229):1054-62.
20. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The lancet*. 2020 Mar 28;395(10229):1054-62.
21. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The lancet*. 2020 Mar 28;395(10229):1054-62.
22. Zhou M, Zhang X, Qu J. Coronavirus disease 2019 (COVID-19): a clinical update. *Frontiers of medicine*. 2020 Apr;14(2):126-35.
23. Zubaida N.M Albarzanji, Thikra Abdullah Mahmood, Entedhar Rifaat Sarhat, Kasim Sakran Abass. Cytokines Storm Of COVID-19 And Multi Systemic Organ Failure: A Review. *Systematic Reviews in Pharmacy*,2020; 11 (10), 1252-1256. doi:10.31838/srp.2020.10.1795.