Study of Human Ferritin and C-Reactive Protein in Patients with COVID-19 in Wasit Province, Iraq

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Abstract
Serum ferritin is an iron storage protein with a primary role of regulating cellular oxygen metabolism, Ferritin has emerged as a key in the immune system, and its role as an acute phase reactant, recent studies have focused on the role of serum inflammatory markers that predict COVID-19 Damage to the organs, such as the liver and spleen, can also cause ferritin levels to rise. In one study of COVID-19 patients, researchers discovered that those with severe and very severe COVID-19 had higher serum ferritin levels, with serum ferritin levels in the very severe COVID-19 population being slightly higher than those in the severe COVID-19 group. CRP is a liver-produced protein that acts as an early indicator of infection and inflammation. Clinical studies have shown that changes in the levels of certain blood markers are related to the severity and mortality of patients COVID.19 . Serum C-reactive protein (CRP) has been identified as an essential marker that varies dramatically in COVID19 patients with extreme symptoms. A study was conducted to study of levels for each ferritin and CRP in COVID.19 patients and compared it with control group according age and gender. The results showed a highly significant of ferritin levels (P value <0.001) between patients and control and non significant Between male and female within patients (P value 0.6 NS) but a highly significant Between male in control & female in patients and Between female in control & male in patients (P value <0.001). Ferritin rustles according to age showed a highly significant for age <40 (P value <0.001). The rustles of CRP showed a highly significant between patients and control and non significant Between male and female within patients (P value 0.093 NS). CRP rustles according to age showed a highly significant for age <40 (P value <0.001).
Keywords: COVID-19 virus, Ferritin, CRP.

1. Introduction

Coronaviruses have one of the largest genome sizes of RNA viruses, ranging from 26 to 32 kilobases. They have distinctive club-shaped spikes that protrude from their surface and, in electron micrographs, resemble the solar corona, from which they get their name.
Coronaviruses, which have been isolated from a variety of species, are a group of large, enveloped, single plus stranded RNA viruses that have previously been associated to acute rhinitis and diarrhea in humans (1,2).
The SARS epidemic in 2002–2003 was associated to a human coronavirus known as SARS-CoV (severe acute respiratory syndrome coronavirus). (3,4)
accompanied by viral amplification, host immune responses become activated, which is supposed to clear the virus and cure the patients. But why a portion of patients had more severe disease development like MODS is still unknown. We hypothesized cytokine storm plays important role in the pathogenesis of severe cases of COVID-19 (5,6).
Serum ferritin is an iron storage protein with the primary role of regulating cellular oxygen metabolism. Ferritin has emerged as a key in the immune system, and its role as an acute phase reactant, recent studies have focused on the role of serum inflammatory markers that predict COVID19(7) . Increased ferritin levels could cause a cytokine storm by exerting direct immunosuppressive and pro-inflammatory effects. The levels of ferritin, a crucial immune response mediator, increase in severe Covid-19 cases. Many individuals with diabetes exhibit elevated serum ferritin levels so that ferritin levels might be a crucial factor influencing COVID-19 severity(8).
The blood ferritin level is a measurement of the amount of iron in the body, and it will increase if there are any disorders that cause significant inflammation. Iron in the body is not the same as ferritinFerritin, on the other hand, is a protein that contains iron and releases it as the body requires it. Ferritin is often contained in the body's cells, with just a small amount circulating in the bloodstream. H and L are the two subunits that make up ferritin, Several studies have indicated that inflammatory factors influence H subunit expression, and that H-ferritin can act as an immunomodulatory molecule

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with both pro-inflammatory and immunosuppressive properties(9).

CRP is a plasma protein produced by the liver cells, called hepatocytes, and its production can be induced by various inflammatory mediators like IL-6. In addition to being a biomarker of acute inflammation, it has recently shown to be associated with chronic inflammations, such as cardiovascular diseases and Type II diabetes mellitus (10) Also, the early expansion of plasma CRP level is shown to increase the likelihood of developing plasma leakage. Hence, CRP level could early predict COVID-19-associated severe pneumonia (11) In this regard, although there are blood markers that appear to be linked with the degree of severity and mortality, the level of CRP was sharply increased in severely SARS-CoV-2 infected patients.9 The pathological, physiological, and diagnostic methods of COVID-19 are in the fact finding stage(12).

2. Material and Methods

Study design

This study was approved by the AL-karama Teaching hospital and External laboratories after fixing their infection, in Wasit provinces/Iraq , All patients (n=40) with COVID-19 enrolled in this study were diagnosed with SARS-CoV-2 infection between December 2021 to May 2022.

The patients age range was from 14 to 70 years , there were 18 male and 22 female, the whole blood collected after diagnosed with SARS-Cov-2(positive nasopharyngeal swab for SARS-Cov-2), and C-reactive protein and CBC reporter and 40 control without COVID - 19, there were 27 male and 13 female, the patients age range was from 9 to 55 years Control samples were for people who did not suffer from blood pressure or other diseases and used covid-19 rapid test to prove not infection COVID -19.

Laboratory examination of blood samples

Approximately 3-5 ml of peripheral blood was obtained with collection tube from the subjects in each group, serum samples were separated by 2000 rpm /20 min centrifugation.

1. Ferritin diagnosis for human serum samples obtained on a Roche/Hitachi cobas c 501 analyzer using the Tina - quant Ferritin Gen.4assay (y) were compared with those determined on a Roche/Hitachi 917 analyzer using the Tina - quant Ferritin assay (x).
2. CRP The results of the CRP tests were taken from the laboratory during the collection of samples in the hospital or from external laboratories, where we were provided with the patient's data after he was previously diagnosed with COVID-19. The data contains all the patient's information and the tests that were conducted for him, including CRP and CBC

3. Statistical analysis

SPSS 22.0 statistical software was used for statistical analysis. Count data were analyzed by the $\chi 2$ test. A P value < 0.05 indicates statistical significance.

4. Results and Discussion

This study was designed to search for ferritin and CRP levels in patients with COVID-19 in 80 samples as a case group compared with control ,used (40 patient 40 control)

Table (1) : The percentage of ferritin patients and controls.

Parameter	Groups	Mean±S.E (ng/mL)	P value
Ferritin	Control	54.71±9.93	<0.001**
	Patients	247.42±21.99	

Furthermore, it was revealed from the statistical analysis there is a higher significant increasing ($p<0.001$) in Ferritin in the serum of SARS-Cov-2 patients than detected in control group, as the mean was (54.71±9.93) ng/mL in control and was (247.42±21.99) in the patients Another study involving 69 patients with severe Covid-19 reported significantly higher ferritin levels in patients with severe disease than in those with nonsevere disease(13).

A possible strategy to decrease ferritin levels might be the treatment with iron chelators. Deferoxamine may be a good candidate since is a non-toxic iron chelator clinically approved by the FDA(14) with decreasing dietary iron should be also considered as they have been shown to modify serum ferritin levels(15).

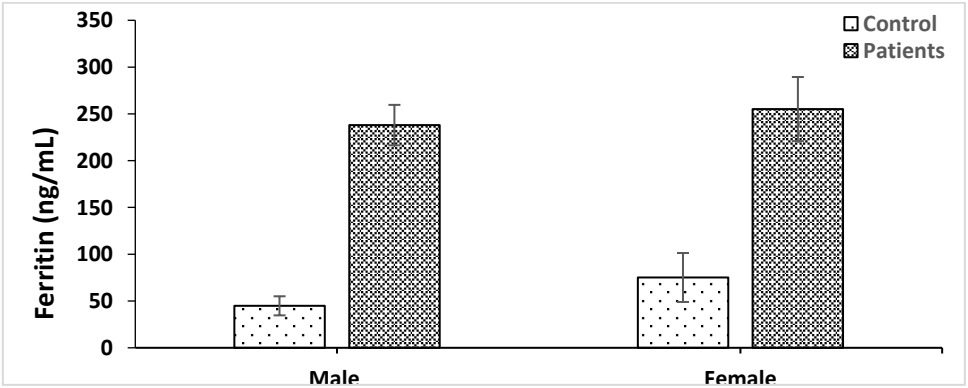
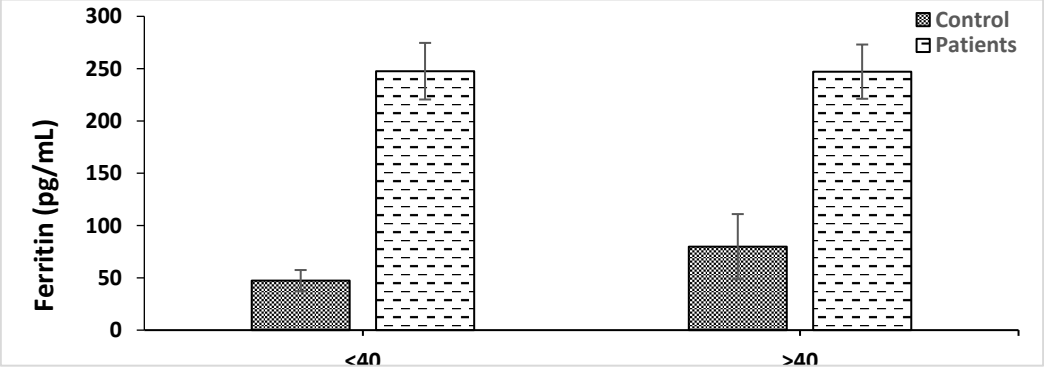


Fig (1): The percentage of ferritin in patients and controls between male and female according to gender

The results of the current study showed that the percentage of ferritin in patients female and male

was higher than that of controls and values of ferritin significantly higher in patients with COVID-19 than in healthy controls (P<0.001) and results showed non significantly (P 0.6 NS) Between male and female within patients.

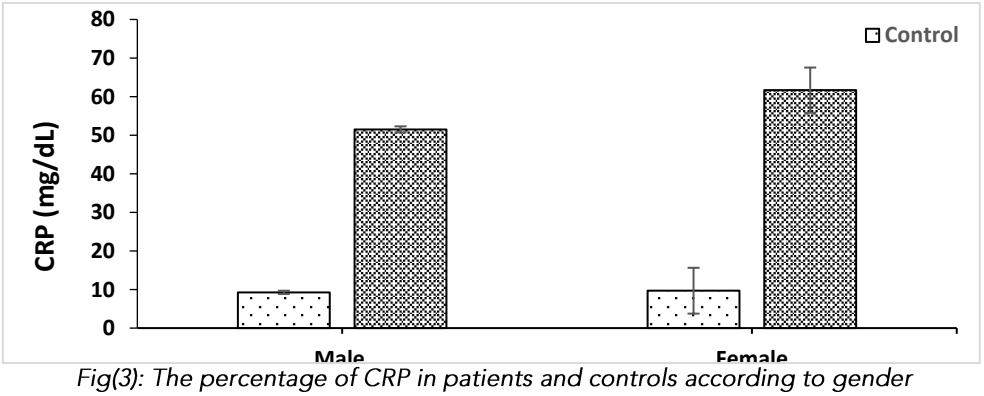


Fig(2): The percentage of ferritin in patients and controls according to age

The results of the current study showed that the percentage of ferritin in patients was higher than that of controls and values of ferritin significantly higher in patients with COVID-19 than in healthy controls (P<0.001) for each age group <40 and >40 in patients. laboratory findings in patients with severe COVID-19 showed data consistent with cytokine storm involving elevated inflammatory markers, including ferritin, which has been associated with critical and life-threatening illness(16).

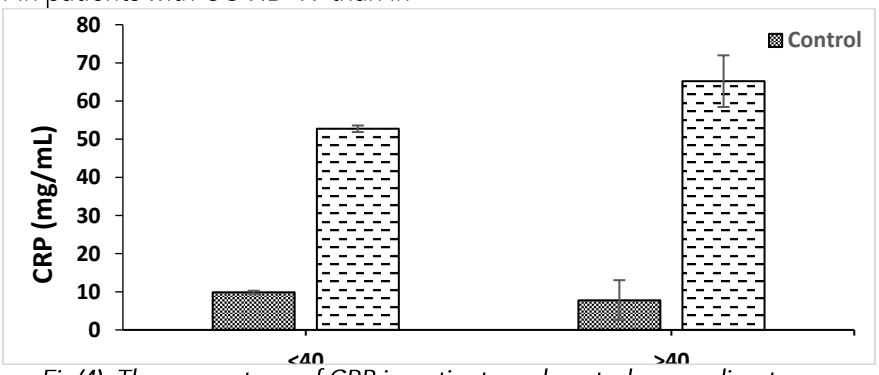
Table (2) : The percentage of CRP patients and controls.			
Parameter	Groups	Mean±S.E (mg/dL)	P value
CRP	Control	9.40±0.38	<0.001**
	Patients	57.10±4.21	

The results of the current study showed that the percentage of CRP in patients was higher than that of controls after personals infection with covid-19. the values of CRP significantly higher in patients with COVID-19 than in healthy controls (P<0.001) .
The elevated level of CRP was witnessed in about 85% of severe COVID-19 patients. It is not only indicating severe infection, but also shown to be a progression of poor outcome of severe infection, since an elevated CRP level was observed in 85% of patients before death(17).This could be suggesting that there is gradual inflammatory reaction in patients with COVID-19(18).



Fig(3): The percentage of CRP in patients and controls according to gender

The results of the current study showed that the percentage of CRP in patients female and male was higher than that of controls and values of CRP significantly higher in patients with COVID-19 than in healthy controls (P<0.001) and results showed non significantly (P 0.093 NS) Between male and female within patients.



Fig(4): The percentage of CRP in patients and controls according to age

The results of the current study showed that the percentage of CRP in patients was higher than that of controls and values of CRP significantly higher in patients with COVID-19 than in healthy controls (P<0.001) for each age group <40 and >40 in patients and values of CRP significantly Between <40 and >40 in patients (0.047).

5. Conclusions

1. The results of the present study showed that an elevated serum CRP, and ferritin were associated COVID-19.
2. Serum ferritin level is a good biomarker of infection in COVID-19
3. to decrease ferritin levels might be the treatment with iron chelators. Deferoxamine, which was approved by the FDA, with decreasing dietary iron should be also considered as they have been shown to modify serum ferritin levels.
4. The utilization of CRP as a biomarker of the extent of hyper inflammatory in body

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