

Serum Ferritin as a Predictive Biomarker for Disease Severity in COVID-19 Patients Presenting to the Hospital: A Case-Control Study

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Abstract

Introduction: COVID-19 is one of the main causes of illness and death. If the variables associated with disease severity and the need for intensive care unit admission can be identified, the approach to managing COVID-19-related diseases may change. Many laboratory tests, including ferritin and C-reactive protein (CRP) levels can be a good way to predict the severity of COVID-19 infection.

Methods: This case-control study included two groups: 55 Patients with COVID-19 who are admitted to the hospital in the Intensive Care Unit (ICU) Imam Hussein Medical City Hospital in Karbala Governorate, and the second group consisted of 28 healthy individuals for comparison. Ferritin concentrations, C-reactive protein (CRP), and some blood variables were measured between the two groups after collecting clinical data and test results, to evaluate the predictive value efficiency.

Results: The study found a significant increase in ferritin levels in patients infected with COVID-19 compared to healthy individuals by $P < 0.05$. It also found an increase in CRP levels compared to healthy individuals, while no significant change was found in Total Serum Bilirubin (TSB) levels in COVID-19 patients. Our study also found a negative, statistically non-significant correlation between serum ferritin levels and each of TSB, CRP, and neutrophils, respectively. ($r = -0.225, r = -0.01, r = 0.04$).

Conclusion: In conclusion, early assessment of serum ferritin levels in patients with COVID-19 contributes significantly to determining disease severity. Therefore, ferritin may play an important role as a simple complementary tool to guide clinical decision-making and treatment. However, we recommend conducting further studies to confirm these results and clarify the precise pathological mechanisms.

Keywords: COVID-19; ferritin; C-reactive protein; lymphocytes.



1. Introduction

The respiratory system is the primary system affected by a virus called Coronavirus Disease 2019 (COVID-19) (Tan et al., 2019). Coughing and sneezing from infected individuals can spread respiratory droplets, which can rapidly disseminate worldwide due to close human contact. The widespread global spread of the disease led to its classification as a pandemic in March 2020 according to the World Health Organization classifications. Cough, fever, shortness of breath, and sepsis are the most common signs and symptoms of COVID-19 (Lino et al., 2021). Approximately 15-20% of COVID-19 patients may experience a condition requiring admission to the intensive care unit (ICU), such as respiratory arrest, shock, or multiple organ failure, although most infections are not fatal (Kerget et al., 2020; Lin et al., 2020). The severity of COVID-19 infection has been shown to be predictable through laboratory variables and inflammatory markers, such as ferritin, decreased albumin, lymphocytes, C-reactive protein, and interleukins (Abdel Fattah et al., 2023). Ferritin is an iron storage protein and an acute phase reactant during inflammation. It is significantly elevated in many diseases, including rheumatoid arthritis, chronic kidney diseases, and autoimmune disorders (Jacobs et al., 1972). A study from China involving twenty cases of COVID-19 patients showed that individuals with severe conditions exhibited a significant increase in serum ferritin levels, with a statistically significant difference between the severe and mild groups. In contrast, another study in New York City demonstrated poor performance of serum ferritin in predicting mortality (Feld et al., 2020; Zhou et al., 2020). Given the variability in the literature regarding the role of ferritin and the conflicting results shown by different studies concerning its association with the disease, this study aimed to evaluate the measurement of ferritin levels in moderate COVID-19 cases and consider it a reliable indicator when requesting laboratory tests, making it an important measurement in disease diagnosis.

2. Materials and Methods

This case-control study included two groups: 55 patients diagnosed with COVID-19 who attended the outpatient unit at Imam Hussein Medical City Hospital in Karbala Governorate, suffering from acute respiratory distress syndrome due to COVID-19, with moderate disease not requiring intensive care admission. The second group consisted of 28 healthy individuals serving as a control group for comparison. Exclusion criteria included cases of anemia due to iron deficiency, malabsorption, all types of thalassemia, hyperthyroidism, leukemia, and rheumatic diseases. The study samples were handled according to World Health Organization guidelines, blood samples were drawn to perform the required analyses, measuring concentrations of ferritin, C-reactive protein (CRP), and some hematological parameters from both groups. Samples were collected from early October 2024 to early March 2025. Data were collected using Excel software and statistically analyzed using SPSS statistical analysis software version 20.0.

3. Results

Figure (1) represents the frequency of males and females infected with COVID-19 as well as healthy males and females, and it is observed that females are higher than males, representing 44% of the research samples Figure (2) represents the frequency of males and females infected with COVID-19 out of a total of 55 samples, and it is observed that the number of females is higher compared to the number of males.

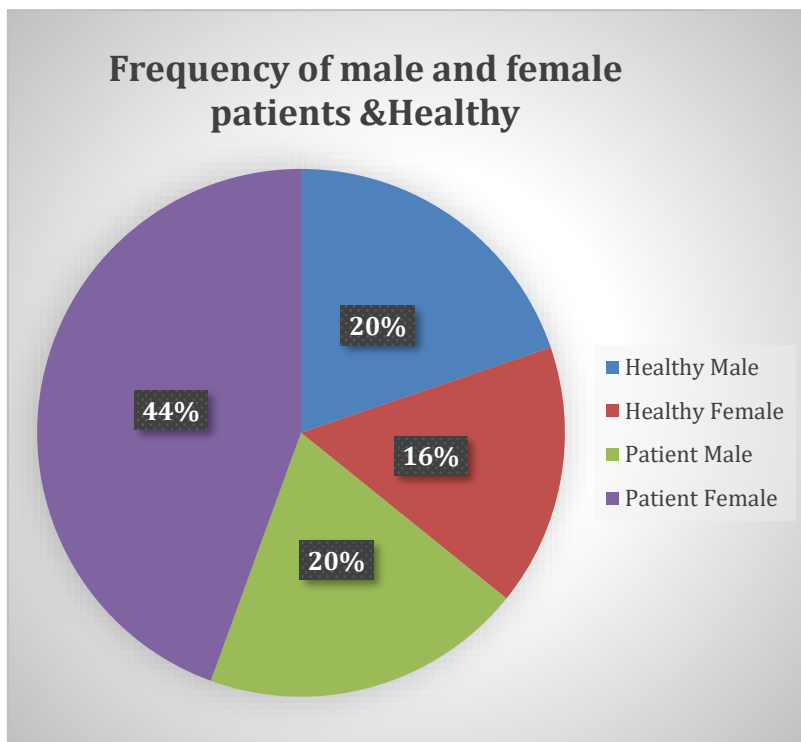


Figure 1. Frequency of male and female patients & Healthy.

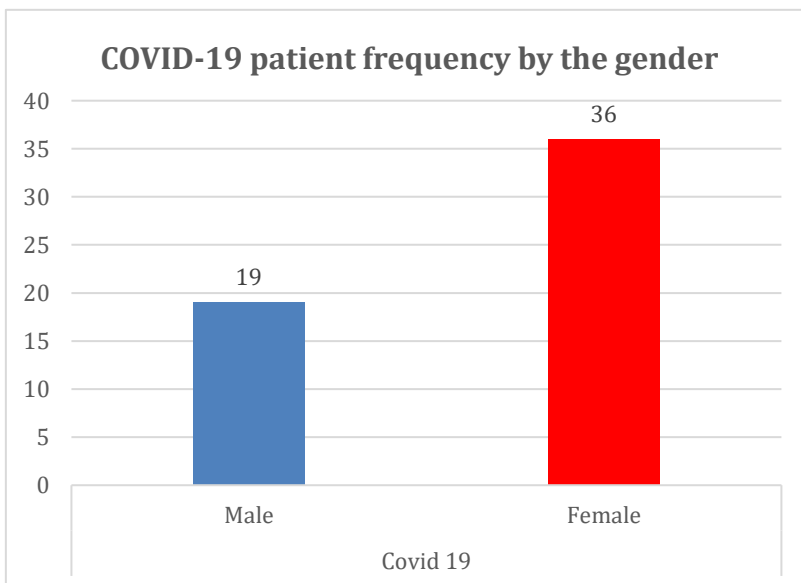


Figure 2. Variation of patients COVID 19 levels by gender for all patients, totaling 55.

Figure (3) represents the repetition of ferritin, CRP, and TSB levels between males and females among healthy individuals and those infected with COVID-19.

Figure (4) represents the variation between ferritin, CRP, and TSB levels among COVID-19 patients within the research samples, which number 55 samples.

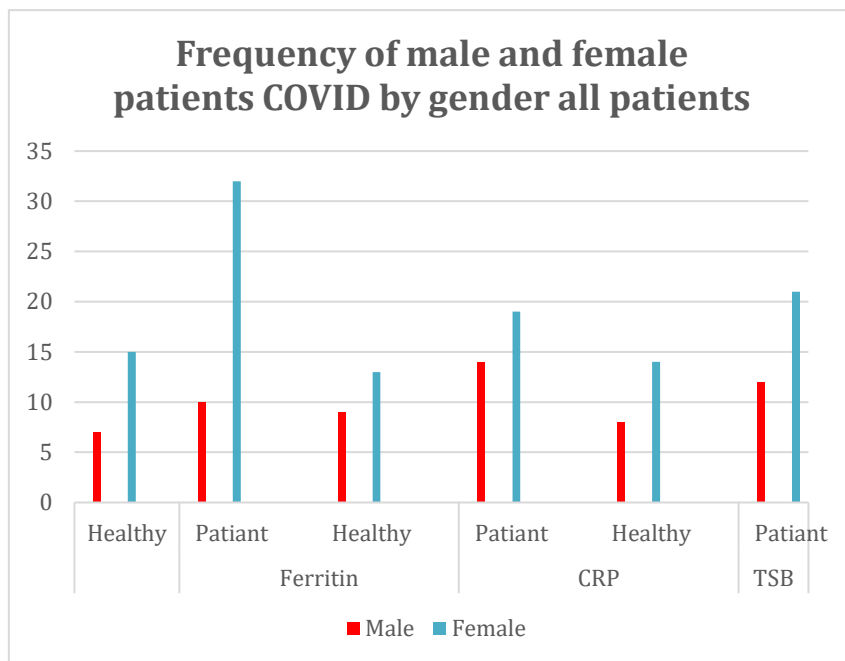


Figure 3. Frequency of male and female patients COVID by gender all patients.

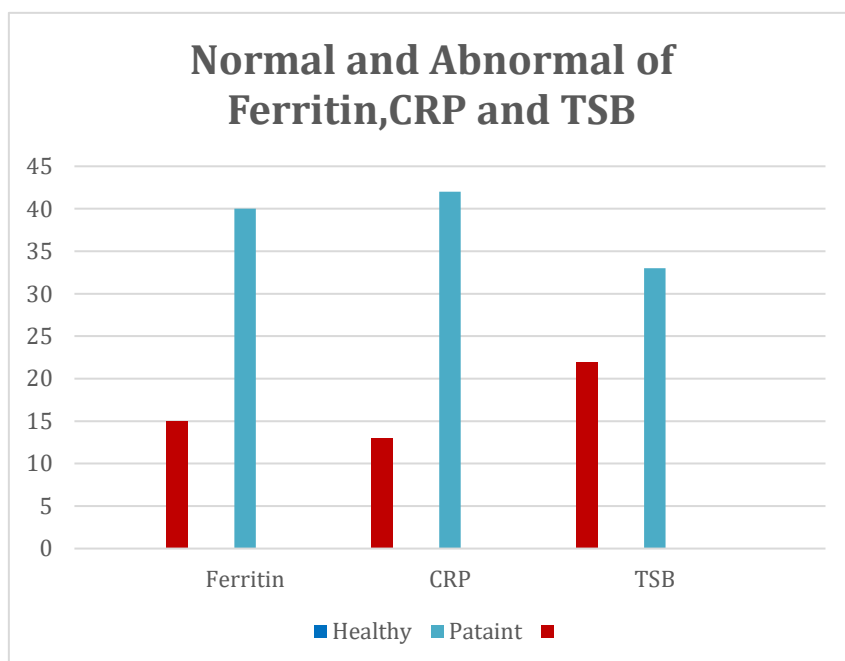


Figure 4. Variation normal and abnormal of ferritin, CRP and Total Serum Bilirubin TSB for all patients, totaling 55.

Table 1. laboratory test results.

| laboratory test | | N | Mean ± S. D | P. value |
|-----------------|---------|----|---------------|----------|
| Ferritin ng/ml | Patient | 55 | 1386.43±148.4 | .002 |
| | Healthy | 28 | 411.95±35.4 | |
| TSB mg/dl | Patient | 55 | 0.63±0.3 | .302 |
| | Healthy | 28 | 0.55±0.3 | |

| laboratory test | | N | Mean ± S. D | P. value |
|-----------------|---------|----|-------------|----------|
| CRP mg/dl | Patient | 55 | 63.87±68.3 | .009 |
| | Healthy | 28 | 21.99±30.9 | |

Table (1) represents the laboratory test results for ferritin and CRP and TSB readings between COVID-19 patients and healthy individuals, with Mean ±SD at P<0.05 significance level.

Table 2. Laboratory parameter results.

| laboratory test | | Gender | Mean± S. D | P. value |
|------------------|---------|--------|----------------|----------|
| S.Ferritin ng/ml | Patient | Male | 1254.64±156.41 | .569 |
| | | Female | 1455.98±104.21 | |
| | Healthy | Male | 354.21±35 | |
| | | Female | 483.02±42 | |
| WBC | Patient | Male | 15.04±3.2 | .358 |
| | | Female | 16.51±4.3 | |
| | Healthy | Male | 7.22±2. | |
| | | Female | 7.44±3.1 | |
| Lymph.% | Patient | Male | 0.26±0.4 | .333 |
| | | Female | 0.23±0.3 | |
| | Healthy | Male | 0.04±0.1 | |
| | | Female | 0.26±0.3 | |
| Platelet | Patient | Male | 209.84±21.7 | .101 |
| | | Female | 228.44±23.3 | |
| | Healthy | Male | 263.94±18.1 | |
| | | Female | 319.08±17.06 | |
| TSB mg/dl | Patient | Male | 0.67±0.4 | .561 |
| | | Female | 0.61±0.3 | |
| | Healthy | Male | 0.57±0.4 | |
| | | Female | 0.53±0.2 | |
| Hemoglobin | Patient | Male | 11.93±1.2 | .418 |
| | | Female | 13.16±1.9 | |
| | Healthy | Male | 13.66±1.6 | |
| | | Female | 12.56±1.7 | |

Table (2) represents the laboratory tests for WBC, Lymphocyte, platelet count, and hemoglobin in COVID-19 patients and healthy individuals, as well as the levels and comparison by gender at P<0.05.

Table 3. Correlation is significant at the P<0.05 level.

| | WBC | Neutro.% | HB | Platelet | TSB mg/dl | CRP mg/dl |
|------------------|-------|----------|-------|----------|-----------|-----------|
| Neutro.% | -.108 | | | | | |
| Platelet | -.004 | -.013 | -.006 | | | |
| S.Ferritin ng/ml | .118 | -.040 | -.054 | -.093 | -.011 | -.225 |

Table (3) shows the correlation relationships between ferritin, blood parameters, CRP, and TSB at P<0.05. The table showed negative correlation relationships, but they did not reach significance at the P< 0.05 significance level between serum ferritin and neutrophils, hemoglobin, platelets, and C-reactive protein, recorded as follows (r = -0.040, r = -0.054, r = -0.093, r = -0.225).

4. Discussion

The aim of this article was to measure ferritin early in COVID-19 patients. As a frequently evaluated biological marker, ferritin is one of the acute phase proteins, in addition to being a mediator in immune dysregulation during cytokine storms in severe infections with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). (Chen et al., 2021; Guan et al., 2020; Yameny, 2021). The severity of COVID-19 infection was positively correlated with blood ferritin levels in the current investigation. International studies have documented similar experiences. For example, twenty severe cases of admitted COVID-19 patients were examined in a single-center observational analysis by Zhou et al. (2020). The results indicated that ferritin, one of the inflammatory markers examined, was significantly higher in very severe COVID-19 cases compared to severe cases (Abdel Fattah et al., 2023; Bozkurt et al., 2021).

Our results showed that the female sex is associated with an increased risk of COVID-19 infection compared to males (Figure 2). This contradicts other studies that found higher infection rates among males, which led to COVID-19-related deaths, according to a study conducted by Nasiri *et al.*, in (2020). Other research from China, Italy, Denmark, and the United States also demonstrated higher mortality rates associated with COVID-19 among males (Gebhard et al., 2020; Shaheen et al., 2020).

Our study relied on a limited number of samples from patients visiting the hospital in the city of Karbala during a specific time period. This may be attributed to lifestyle patterns more common among males (such as smoking, lower rates of handwashing, and obesity), in addition to comorbidities (Dahan et al., 2020; Kragholm et al., 2021). Or to underlying mechanisms in immune responses related to sex chromosomes. Studies conducted by Gebhard et al. (2020) which investigated clinical and epidemiological gender differences in COVID-19 in China and Europe, showed no statistically significant differences in the number of recorded cases between males and females. However, hospital admission records, progression to severe cases, and mortality rates were significantly higher among males (Abdel Ghaffar et al., 2022; Bianconi et al., 2022). Recent studies have evaluated several serum biomarkers, including lymphocyte count, C-reactive protein (CRP) levels, and erythrocyte sedimentation rate (ESR), to predict disease severity (Adkinson et al., 2020). Furthermore, in the very early stage of COVID-19. (Sayit et al., 2021) observed elevated CRP and ESR levels and suggested that these could be used to predict the occurrence of severe disease before the appearance of computed tomography imaging results. However, in the current study, we found that the variation in serum ferritin levels can be considered an important indicator for predicting the presence of COVID-19 infection.

5. Conclusions

In conclusion, early assessment of serum ferritin levels in patients with COVID-19 contributes significantly to determining disease severity. Therefore, ferritin may play an important role as a simple complementary tool to guide clinical decision-making and treatment. However, we recommend conducting further studies to confirm these results and clarify the precise pathological mechanisms.

6. Recommendation

We recommend measuring serum ferritin levels at the onset of symptoms in patients infected with COVID-19 as it is a biomarker that often appears with the infection, and because it is a low-cost test that is readily available in most laboratories.

7. Acknowledgement

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8. Conflicts of interest

No conflict of interest.

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