

Correlation of ferritin with D-dimer in obese Iraqi male patients with COVID-19 disease

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ABSTRACT

BACKGROUND: This study aimed to assess the levels of ferritin and D-dimer in overweight Iraqi men who had COVID-19, a disease caused by the SARS-CoV-2 virus that spread across six continents and over 200 countries, regions, or territories since 2019. The study also examined the possible relationship between these biomarkers. COVID-19 affected men more than women, and people with chronic conditions more than healthy ones, with different symptom severity.

Methods: We reviewed clinical and laboratory data from 100 male COVID-19 patients admitted to Al-Amal Hospital in Najaf, Iraq, between September and December 2021. We used real-time PCR to confirm the infection. We also recruited 50 healthy subjects who tested negative for COVID-19 as a control group. We performed general examinations and measured D-dimer, ferritin, and body mass index levels. We compared these levels between obese and non-obese patients and controls..

Results: A higher level of ferritin and D-dimer was found in Covid-19 patients compared to healthy controls. The statistical significance for ferritin was b value ($p < 0.01$) and for D-dimer ($p < 0.03$). There was also a significant correlation between D-dimer and ferritin in Covid-19 cases.

Conclusions: There is a correlation between the levels of ferritin and D-dimer in individuals diagnosed with COVID-19, particularly obese individuals who have high levels that raise the chance of mortality. This outcome is associated with the failure of multiple organs function in human body resulted from COVID-19 infection and exacerbation of injury, such as liver, kidneys and respiratory system.

Keywords: COVID-19, SARS-CoV-2, male COVID-19 Patients, Iraq COVID-19 Patients, obese patients, D-dimer, ferritin

INTRODUCTION

Fever, breathing difficulty, diarrhea and headache are the most common symptoms that appeared in patients infected with Covid 19 in late 2019, Wuhan, China experienced an outbreak of a novel coronavirus disease, which presented with a wide range of symptoms, In 188 countries and territories There are more than 600 million known cases of the illness, with more than 6.26 million deaths as of 14 May 2022 (1). Due to the global spread of new coronavirus 2 (SARS-CoV-2) and global health concerns, COVID-19, which is caused by SARS-CoV-2, has emerged as one of the most challenging obstacles in many nations. On March 11, 2020, the WHO announces a worldwide pandemic (2). Non-sense positive RNA viruses called coronaviruses That cause That cause respiratory and gastrointestinal illnesses in both humans and animals. (3) A coronavirus is a single-stranded, positive-experience RNA virus belonging to the Coronavirinae subfamily of the Coronaviridae group of viruses in the Nidovirales order.(4). Coronaviruses are encapsulated through favorable situations RNA viruses have spike-like projections on their floor and variety in diameter from 60 nm to 134 nm, giving them a crown-like appearance. then the time coronavirus, at the back of the electron microscope(5)

Coronaviruses, belonging to the Nidovirales order and Coronaviridae family, are known to infect humans and other mammals on a regular basis. (6). D-dimer is a biomarker that belongs to the fibrin degradation product (FDP) family, which is released into the bloodstream. Once the blood clot undergoes fibrinolysis, it is broken down and results in the attachment of fibrin D-dimer moieties to a cross-link. According to the researchers, prolonged levels of D-dimer serve as an indication of pulmonary complications and potentially fatal thromboses. However, there is currently no conclusive threshold of D-dimer levels that can be attributed to mortality. (7) Studies have shown that there is a close association between people with Covid 19 and a high rate of blood clots and a high rate of D-dimer, and the study has proven that patients who have a D-dimer rate > 1000 ng/ml are more likely to die 20 times more than those who have a D-Dimer less than 1000 (8) Ferritin is a blood protein that contains iron, The serum level depicts the typical amount of iron and aids in the identification of iron deficiency, Studies have examined the levels of ferritin and the risk of high levels and its association with liver cell damage. During viral infection, the level of ferritin rises in the blood and may indicate viral replication. (9) Since ferritin is a hallmark of inflammation in obesity, central obesity-related inflammation lowers iron levels and raises levels of free fatty acids.(10) The research addressed the role of information systems, collecting them, and measuring the results of ferritin levels to determine whether ferritin is an indicator of death for Covid-19 patients.(11)

According to studies, patients with fatty liver disease and those who are overweight tend to have higher ferritin levels. Iron status may not be as closely associated with the appearance of harmful metabolic and inflammatory consequences of overweight

and obesity as high ferritin levels. Our findings provide fresh insight into how to interpret serum ferritin levels in obese male adolescents since it seems that serum ferritin rises more in correlation with liver fat and inflammation than does body iron reserves. Subsequent investigations are required to ascertain the extent of liver disease and to establish the clinical utility of serum ferritin as a biomarker for young individuals afflicted with nonalcoholic fatty liver disease.(12)

DEFINITION OF OBESITY

Obesity is characterized as a chronic disease in which the body has collected an excessive amount of body fat, which has negative repercussions. Since ferritin is a hallmark of inflammation in obesity, central obesity-related inflammation lowers iron levels and raises levels of free fatty acids. When a person's BMI is 30 kg/m² or higher, they are called obese.(13) Obesity raises the incidence of a number of illnesses, including osteoarthritis, several types of cancer, heart disease, type 2 diabetes, and obstructive sleep apnea. (14)Based on BMI, which is determined as follows, obesity may be categorized into the following groups; BMI is equal to Weight (kg)/Height (m²). Individuals can be categorized as underweight if their body mass index (BMI) is below 18.5 kg/m². A body mass index (BMI) falling between 18 and 24.9 kg/m² is regarded as being within the standard weight category. Individuals whose BMI ranges from 25 to 29.9 kg/m² are classified as being overweight, whereas those whose BMI is equal to or greater than 30 kg/m² are categorized as being obese. Class III obesity, also known as morbid obesity, is characterized by a body mass index (BMI) of 40 or higher. According to the established criteria, a body mass index (BMI) ranging from 30 to 35 kg/m² is classified as class I obesity, while a BMI ranging from 35 to 40 kg/m² is classified as class II obesity. Additionally, a BMI exceeding 40 kg/m² is classified as class III obesity. (15)

MATERIALS AND METHODS

In this research, 50 COVID-19-positive Iraqi patients took part. Among all patients tested, only 50 passed the biochemical analysis. The patients' mean BMI was 33.44±4.76, and their ages varied from 45 to 65. HbA1c was 6.08±0.8% and random blood sugar was 130.12±20.14 mg/dL, respectively. During the months of September through December 2021, At the Al-Amal Hospital in Najaf, Iraq, these patients were identified as COVID-19. Clinical signs, PCR results, and biochemical testing were used to diagnose the patient. The present research excluded individuals who were female, had high blood pressure, had infections or endocarditis, had cardiac conditions, belonged to non-Arab ethnic groups, or had thyroid disorders.

The control group consisted of fifty participants. Their mean BMI was 22.94 ±3.15, and they shared the patients' approximate age. The study findings indicate that the average values for random blood sugar readings and HbA1c levels were 101.9 ± 11.18 mg/dL and 5.03± 0.63%, respectively. The study excluded individuals who displayed symptoms of anemia and those who presented with obvious systemic illness.

According to the recommendations of the World Health Organization (WHO), body mass index (BMI) is calculated by dividing the weight in kilograms by the square of the height in meters (kg/m²). WHO has classified BMI into different categories based on the health risks associated with different levels of body fatness. A normal BMI range is 18 to 25 kg/m², while a BMI of more than 30 kg/m² is considered obese.

Five milliliters of venous blood were collected from each control subject using a disposable needle and plastic syringe. The process of blood separation involves the utilization of a pair of gel tubes and a pair of anticoagulant tubes. After a 15-minute period of coagulation at ambient temperature, the blood sample underwent centrifugation at a force of 3000 times the acceleration due to gravity for a duration of 5 minutes. Subsequently, the serum that was obtained was meticulously isolated and subsequently relocated into fresh, disposable tubes.

The research employed contingency table analysis, more specifically the χ test, to validate the correlation between nominal variables. Furthermore, the Student's T-test was employed to evaluate differences in metric variables across diagnostic groups. The research utilized Spearman's rank order correlation coefficients and Pearson's product moment to establish the relationships among the variables. A two-tailed test was conducted to determine statistical significance using a significance level of 0.05. The statistical procedures were performed utilizing IBM SPSS version 26 software on a Windows operating system.

RESULTS AND DISCUSSION

This study found that there is no significant differences in age and gender between COVID-19 patients and control group as shown in table (1).

Table 1.Demographic and clinical data of healthy controls (HC) and COVID subjects

Parameters	Obese with COVID-19 Mean±SD	Healthy group Mean±SD	P value
Total number	50	50	----

Male	50	50	----
Age (Year)	58.3±6.17	48.13±7.93	0.913
BMI (kg/m ²)	33.44±4.76	22.52±2.03	0.001
SBP (mmHg)	144.49±10.10	120.35±5.74	0.001
DBP (mmHg)	8.13±1.06	7.91±0.63	0.701
SpO ₂ %	90.64±3.71	98.50±0.69	

The study revealed that COVID-19 patients exhibited significantly elevated levels of D-dimer ng/ml compared to the healthy control group ($P < 0.01$). Additionally, the ferritin ng/ml levels in COVID-19 patients were observed to be significantly higher than those in the healthy group ($P < 0.03$).

Table 2. Ferritin and dimer levels in obese male patients infected with Covid-19 and the control group

Parameters	Mean±STD Patients	Mean±STD Controls	P-Value
D-dimer ng/mL	1228.6±212.63	279.53±43.96	<0.01*
Ferritin ng/mL	830.33±191.81	106.5±22.73	0.03*

The global community is currently experiencing the impact of the COVID-19 pandemic, caused by a highly contagious illness. Due to its unique infectiousness and high mortality rate, the pathogenesis of COVID-

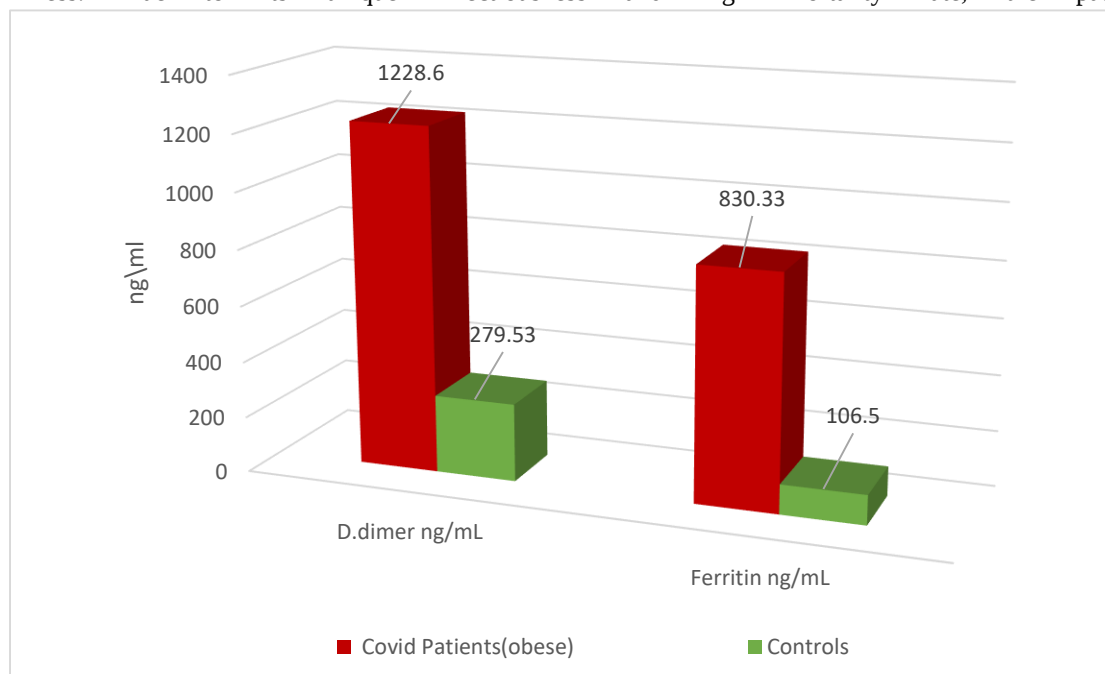


Figure 1. Ferritin and dimer levels in obese male patients infected with Covid-19 and the control group

19 remains poorly understood.

Research has uncovered intricate and noteworthy impacts of COVID-19 on diverse human physiological structures and functions, encompassing the respiratory, immune, digestive, circulatory, hepatic, renal, and hematological systems. (16).

A study was conducted in the United States of America on patients with Covid-19 disease, and the d-dimer level was measured in the 1065 patients, and after comparing them with the normal levels, it was found that there is a significant percentage of the p-value up to 0.001, which confirms that the d-dimer analysis is one of the important indicators To diagnose the disease because it was found high in patients with Covid-19 disease, and the deaths counted by the research amount to 313 of the infected, or approximately 29.4%, and that many patients who need admission to the intensive care unit have very high d-dimer reading levels Relative to other patients (17)

A scientific research discussed the results of a d-dimer for its study on Covid 19 patients when it collected 150 samples for the study from patients with Covid 19 disease with an average age of 50 years, and the number of obese patients was 28, or 18.7%, whose body mass exceeds 30 for BMI (18)

A group of researchers found that there is a relationship between obese males and a high percentage of ferritin and iron in the blood as a result of excess weight and different eating methods, when they took into account in the study the body mass index and gender, which they reached that only males had high rates of ferritin and Iron overload, From this, we learn about the danger of obesity and weight gain affect ferritin levels. Not to mention, if we pay attention to the level of risk that becomes when quail are infected with the Covid-19 virus, then the level of risk doubles.(19)

In a separate investigation, the ferritin level was utilized as a metric for mortality in a cohort of Covid-19 patients. Specifically, the study examined samples from patients with primary infection and advanced illness, comparing them to a control group. The results indicated that individuals with elevated ferritin levels (20) were more likely to experience mortality. The SARS-CoV virus gains entry into human cells predominantly through the angiotensin-converting enzyme 2 (ACE2) receptor. This receptor plays a crucial role in enabling the virus to cause direct cellular harm during the course of infection.(21)

Correlation of ferritin with D-dimer

Table 3. the Correlation of ferritin with D-dimer

Parameter	D-dimer	ferritin
D-dimer	1	0.51*
Ferritin	0.51*	1

* The correlation has a statistically significant value at the 0.01 level, with a two-tailed test.

Ferritin and D-dimer had a substantial inverse relationship, according to the findings. This exhibits the intimate relationship between ferritin and the di-dimer, which is shown by the value of 51. The findings of the study suggest a noteworthy correlation between the levels of ferritin and D-dimer in individuals who have contracted severe COVID-19.(22) Assessment the Correlation of D-dimer and Ferritin Level in Patients Infected with Covid-19, an Iraqi study done in the governorate of Anbar A research on the levels of D-dimer and ferritin demonstrated their strong ties and linkage in patients with Covid-19, and the study's findings corroborated those of the 193 male patients who made up the study's sample of male patients (23). this study sought to determine the serum concentrations of IL-6, D-dimer, ferritin, and CRP as well as to examine the correlation between these concentrations and the severity of the illness. The study's results indicate a correlation between Marker levels and the severity of the illness. The study further elucidated a correlation between ferritin and D-dimer concentrations.(24) This study investigated the correlation between the concentrations of ferritin and D-dimer and the impairment of dissemination capabilities and the onset of COVID-19 pneumonia. The observed levels of Ferritin and D-dimer were significantly elevated beyond anticipated values.(25)

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