

## Serum ferritin as a guide for CT chest indication in patients suspected to COVID-19

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### Abstract

**Background:** The coronavirus disease 2019 (COVID-19) has rapidly developed into a pandemic. Increased levels of ferritin due to cytokine storm and secondary hemophagocytic lymphohistiocytosis were found in severe COVID-19 patients. Therefore, the aim of this study was to evaluate the role of ferritin level as indicator for positive chest CT. scan.

**Patients and methods:** 185 Patients involved through February to June. In this study, the blood sample was collected in patients suffering from fever, sore throat with or without dry cough. Then S.ferritin was estimated and after that we did chest-scan.

**Result:** 164 patients were positive findings for chest- Cscan finding at the level from 10-410 ng/ml of ferritin.

**Conclusion:** Serum ferritin is a valuable marker that can aid in triaging and determining the need for CT chest imaging in suspected COVID-19 cases. However, its use should be integrated with a broader clinical assessment to ensure appropriate and effective management

**Keywords:** Serum ferritin; CT chest indication; COVID-19; ICU and cytokine storm

### 1. Introduction

The text further elaborates on the significance of ferritin levels and their relationship with the severity of COVID-19, particularly among those with underlying health conditions. Here's more detail <sup>(1,2)</sup>:

**Role of Cytokine Storm:** COVID-19 triggers a dysfunctional immune response, referred to as a "cytokine storm," which shares similarities with severe influenza. During the progression of the disease, inflammatory cytokines such as TNF- $\alpha$ , IL-6, IL-12, and IL-8 are released in large amounts. These cytokines contribute to inflammation and can lead to life-threatening complications, including acute respiratory distress syndrome (ARDS) and systemic organ failure <sup>(3)</sup>.

• **Biomarkers of Disease Severity:** Elevated levels of biomarkers such as serum ferritin, D-dimer, lactate dehydrogenase, and IL-6 are observed as the disease worsens. These biomarkers can indicate the risk of mortality, serving as warning signs that patients may be at a higher risk for severe disease outcomes <sup>(4,5)</sup>.

**Hyperferritinemia and Its Implications:** Ferritin, a protein that stores iron, is known to increase during inflammatory responses. In COVID-19, hyperferritinemia is strongly linked to severe disease and poor prognosis. Excessive ferritin levels often correlate with a need for intensive care unit (ICU) admission and higher mortality rates. Ferritin can be considered a biomarker for identifying high-risk patients, helping guide medical interventions aimed at controlling inflammation <sup>(6)</sup>.

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**Ferritin as an Immune Mediator:** Ferritin acts as a mediator of immune dysregulation, particularly in cases of extreme hyperferritinemia. In high concentrations, ferritin can have both immune-suppressive and pro-inflammatory effects, contributing to the cytokine storm. The role of ferritin in immune responses is particularly critical because it may promote an exaggerated inflammatory reaction, which can worsen the disease <sup>(7)</sup>.

**Impact of Diabetes on Ferritin Levels:** Studies have shown that individuals with diabetes often exhibit elevated serum ferritin levels. This elevation is particularly concerning because individuals with diabetes are more likely to experience severe complications if infected with COVID-19. The combination of high ferritin levels and pre-existing conditions like diabetes creates a heightened risk for adverse outcomes in COVID-19 patients <sup>(8)</sup>.

**Small-Scale Studies and Future Research:** Although the evidence linking ferritin levels to COVID-19 severity is compelling, many of the studies conducted so far have been limited in scope, with small sample sizes or based in single centers. More extensive, multi-center studies are needed to validate these findings and strengthen the evidence supporting ferritin as a predictive marker for disease progression and outcome <sup>(7)</sup>.

## 2. Material and methods

### 2.1. Study design

A 185 Patients including in this study. They clinically suffering from fever, sore throat with or without dry cough, the blood sample was collected from them , serum separated then serum ferritin level was measured and after that we did chest- CT-scan to evaluate the positive findings in relation to ferritin level.

### 2.2. Selection criteria

All patients with suspected clinical features of covid-19 including in study and no exclusion criteria in this study the studies were those that investigated ferritin and its clinical relevance in patients diagnosed with COVID-19. The exclusion criteria were as follows: review articles; case reports; patients age (20-60) year.

### 2.3. Data analysis

The difference in Serum ferritin level between the study groups was evaluated using the Student's t-test via the Statistical Package for the Social Sciences (SPSS), version 22. Pearson's correlation coefficient was employed to evaluate the potential link between various biochemical indicators and both age and BMI of the patients.

## 3. Results

### 3.1. The Distribution of Patients According to Socio-demographic Characteristics

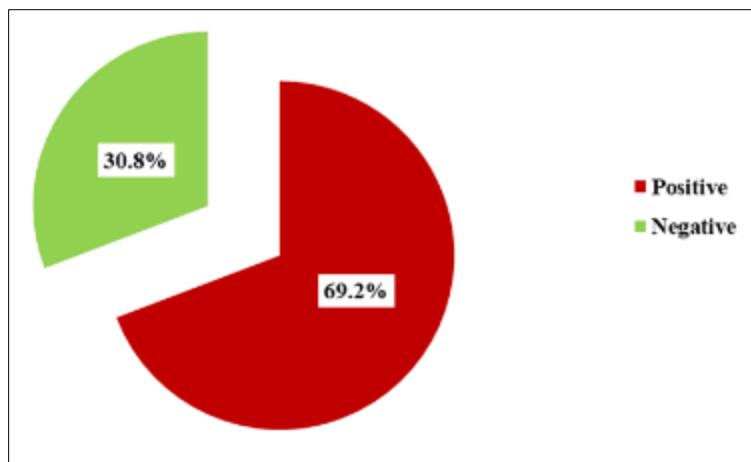
Table 1 shows distribution of patients according to socio-demographic characteristics including (age and gender).

**Table 1** The Distribution of patients according to socio-demographic characteristics (N=185)

Study variables		
Age	(56.16 ± 14.93)	(15-90)
Gender		
Male	71	38.4%
Female	114	61.6%
Total	185	100.0%

### 3.2. The Distribution of Patients According to CT Results

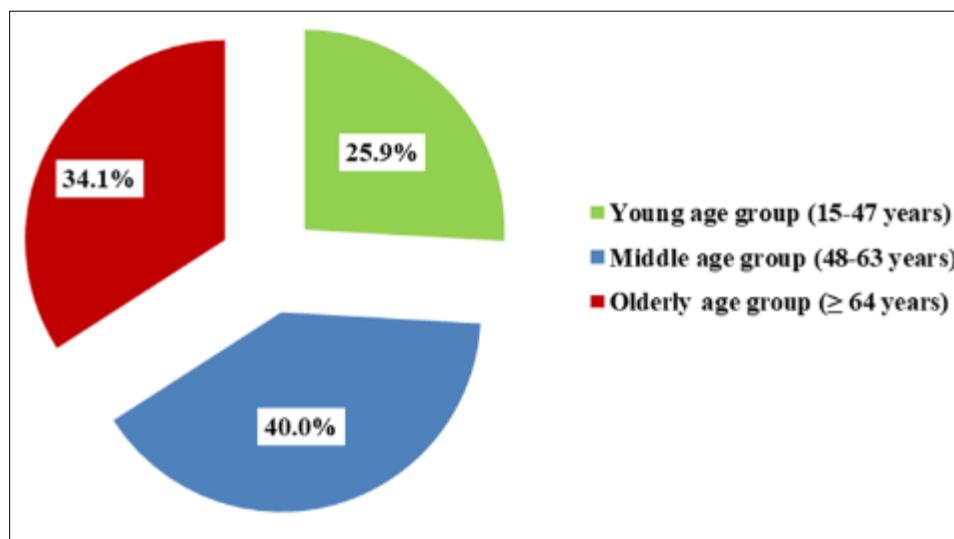
Figure 1 shows distribution of patients according to CT scan results including (Positive or negative) . Positive CT scan occur in about (N=128, 69.2%) of study patients.



**Figure 1** Distribution of patients according to CT scan results

### 3.3. The Distribution of Patients According to Age group

Figure 2 shows distribution of patients according to age group including (15–47 years old (young age group), 48–63 years old (middle age group) and  $\geq 64$  years old (elderly age group). Majority of patients presented with middle age group (N=74, 40.0%).



Mean  $\pm$  SD and range of serum ferritin level among study patients

**Figure 2** Distribution of patients according to age group

Table 2 shows Mean  $\pm$  SD and range of serum ferritin level among study patients. Mean serum ferritin level was (389.21  $\pm$  362.32) with minimum value (10) and maximum value (2000).

**Table 2** Mean  $\pm$  SD and range of serum ferritin level among study patients (N=185)

Study variables	N	Mean $\pm$ SD	Range
Serum ferritin	185	(389.21 $\pm$ 362.32)	(10-2000)

Mean  $\pm$  SD and Range of Serum Ferritin Level Among Study Patients with Positive CT by Each Age Group and Gender

Table 3 shows Mean  $\pm$  SD and range of serum ferritin level among study patients with positive CT by each age group and gender.

**Table 3** Mean  $\pm$  SD and range of serum ferritin level among study patients with positive CT by each age group and gender

Study variables	Study group	N	(Mean $\pm$ SD)	Range
Serum ferritin	Total patients with positive CT scan	128	(453.30 $\pm$ 390.25)	(13-2000)
Serum ferritin	Male with young age group (15-47) years	16	(551.18 $\pm$ 455.84)	(130-2000)
Serum ferritin	Male with middle age group (48-63) years	17	(573.94 $\pm$ 470.85)	(176-2000)
Serum ferritin	Male with elderly age group ( $\geq$ 64) years	17	(546.82 $\pm$ 387.64)	(90-1500)
Serum ferritin	Female with young age group (15-47) years	10	(224.20 $\pm$ 95.06)	(13-350)
Serum ferritin	Female with middle age group (48-63) years	38	(387.87 $\pm$ 394.53)	(98-2000)
Serum ferritin	Female with elderly age group ( $\geq$ 64) years	30	(439.00 $\pm$ 331.65)	(150-1400)

Mean  $\pm$  SD and Range of Serum Ferritin Level Among Study Patients with Negative CT by Each Age Group and Gender

Table 4 shows Mean  $\pm$  SD and range of serum ferritin level among study patients with negative CT by each age group and gender.

**Table 4** Mean  $\pm$  SD and range of serum ferritin level among study patients with negative CT by each age group and gender

Study variables	Study group	N	Mean $\pm$ SD	Range
Serum ferritin	Total patients with negative CT scan	57	(245.27 $\pm$ 235.52)	(10-1130)
Serum ferritin	Male with young age group (15-47) years	10	(224.00 $\pm$ 122.56)	(20-400)
Serum ferritin	Male with middle age group (48-63) years	5	(508.20 $\pm$ 249.72)	(153-778)
Serum ferritin	Male with elderly age group ( $\geq$ 64) years	6	(307.16 $\pm$ 196.65)	(145-650)
Serum ferritin	Female with young age group (15-47) years	12	(141.83 $\pm$ 173.43)	(10-540)
Serum ferritin	Female with middle age group (48-63) years	14	(207.07 $\pm$ 279.91)	(10-1130)
Serum ferritin	Female with elderly age group ( $\geq$ 64) years	10	(275.55 $\pm$ 268.27)	(78-1000)

Table 5: The mean differences of serum ferritin according to CT scan results (positive and negative) among all study patients. There were significant differences between means of serum ferritin () according to CT scan results.

**Table 5** The mean differences of serum ferritin (ng/mL) according to CT scan results

Study variable	CT	N	Mean	SD	t-test	P-value
Serum ferritin (ng/mL)	Positive	128	453.30	390.25	4.473	<0.001*
	Negative	57	245.27	235.52		

\*P value  $\leq$  0.05 was significant

#### 4. Discussion

Ferritin is an acute-phase reactant, and its concentrations increase during systemic inflammation, exemplified by the hyperinflammatory state (cytokine storm) observed in COVID-19.

- Correlation with Illness Intensity: Increased ferritin levels are associated with severe consequences in COVID-19, including as respiratory distress and multi-organ failure.

The role in guiding CT chest indications: Elevated ferritin levels indicate a severe inflammatory response and may signify an increased chance of substantial pulmonary involvement (e.g., ground-glass opacities or consolidation).

- Imaging Prioritisation: Ferritin levels can assist in prioritising patients for CT imaging, particularly when symptoms are ambiguous or complications require assessment, especially in resource-constrained environments.

Benefits of Serum Ferritin Surveillance:

- General yet Indicative: Although not exclusive to COVID-19, increased ferritin levels forecast severe illness and enhance clinical and radiological assessments.
- Cost-Effectiveness: The measurement of ferritin is more economical and readily available compared to CT imaging.

Constraints and Considerations, Non-Specific Character: Ferritin concentrations may be increased in numerous circumstances, diminishing its specificity in directing CT imaging.

- Complementary Application: Ferritin must not supplant clinical judgement and should be utilised alongside other diagnostic tools (e.g., CRP, D-dimer) to inform decisions on CT imaging(16).

Clinical Scenarios, Mild Symptoms with raised Ferritin: Patients with mild symptoms and raised ferritin levels may benefit from prompt CT imaging to identify subclinical pulmonary involvement.

Exacerbating Symptoms with Elevated Ferritin: In deteriorating instances with elevated ferritin, CT can aid in evaluating the advancement of pulmonary involvement and guide therapeutic strategies (17).

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## 5. Conclusion

Within the context of suspected instances of COVID-19, serum ferritin is a helpful measure that can assist in the process of triaging and determining whether or not CT chest imaging is required. In order to guarantee suitable and efficient care, however, its utilisation must be incorporated into a more comprehensive clinical evaluation.

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### Compliance with ethical standards

#### *Disclosure of conflict of interest*

No conflict of interest to be disclosed.

#### *Statement of ethical approval*

The Ethical Committee in Hammurabi College of Medicine authorized the protocol.

#### *Statement of informed consent*

Informed consent was obtained from all individual participants included in the study. Following the elucidation of the study's objectives and the acquisition of written informed consent from all participants, baseline demographic and clinical data were gathered through interviews and documented using the study questionnaire.

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