

Serum Ferritin Level and Covid-19 Severity – Is There a Link?

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ABSTRACT

Background: The outcomes of covid patients vary based on age, gender, co-infections, comorbid conditions and biochemical and hematological parameters.

Objectives: To evaluate the outcomes of COVID-19 patients with Ferritin as a predictor of severity.

Study Design: Cross sectional / Observational study.

Place and Duration of Study: The study was performed in the Department of Medicine at Khyber Medical College/Teaching Hospital Peshawar from April 2021 to June 2021.

Methodology: A total of 90 patients were included in the study. Patients were divided into two groups; FM group included the Ferritin levels of the patients with the Mild to Moderate Illness. FS group included the Ferritin levels of the patients with the severe illness. All information was recorded using proforma and analysed on IBM SPSS for MacBook, Version 26.0.

Results: Linear regression analysis showed that ferritin level was a significant predictor of disease severity (Adjusted R Square = .880). Ferritin was 105.70 ± 43.19 (ng/ml) for FM group and 725 ± 125.19 (ng/ml) for FS group.

Conclusion: Ferritin levels might predict the disease severity effectively if done early on.

Keywords: Ferritin; Hospitalized Patients; Biomarker

INTRODUCTION

COVID-19 infection has played havoc by rapidly spreading across continents, infecting large populations. The virus infects by attaching itself to the angiotensin-converting enzyme 2 (ACE-II) receptor.¹ Ferritin is an acute phase reactant and a major intracellular iron storage protein. It is raised in many inflammatory conditions.²

It is observed that elevated ferritin levels have poor prognosis in hospitalized patients.³ Various studies have correlated elevated ferritin levels and other pro-inflammatory markers in COVID-19 to disease severity, poor outcomes, and mortality/morbidity.⁴⁻⁶ The utility and ability of ferritin levels as a marker to predict disease severity has been reported but not fully understood.⁷ We report here on a descriptive analysis of patients admitted for COVID-19, evaluating Leucocyte Counts, C-Reactive Protein, D-Dimer, and Ferritin values amongst other baseline investigations.

The aim of our study is to evaluate the outcomes of patients having COVID-19 for their disease severity with Ferritin as a marker for the prediction.

METHODOLOGY

The cross-sectional study was performed in the Department of Medicine at Khyber Medical College/Teaching Hospital Peshawar from April 2021 to June 2021 to evaluate the outcomes of patients having COVID-19 for their disease severity with Ferritin as a marker for the prediction. A total of 90 patients were included in the study by confirming results on RT-PCR. Patients were divided into two groups: FM Group for Mild to Moderate Disease and FS for Severe Disease. FM group includes the Ferritin levels of the patients with the Mild to Moderate Illness. Mild to Moderate Illness is fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhoea, loss of taste and smell, some shortness of breath/dyspnoea on

exertion and $\text{SpO}_2 \geq 94\%$ on room air. FS group includes the Ferritin levels of the patients with the severe illness. Severe Illness is $\text{SpO}_2 < 94\%$ on room air, respiratory rate > 30 breaths/min, $\text{PaO}_2/\text{FiO}_2 < 300$ mm Hg, or lung infiltrates $> 50\%$. Blood was taken and analyzed at the Hospital Laboratory via Cobas 6000 E 501 analyzer. The following parameters were checked: Serum Ferritin, C-Reactive Protein, D-Dimers and White Blood Cells. All confounding variables were controlled by exclusion criteria. Bias was controlled by following strict inclusion criteria for patient selection. All information was recorded using proforma and analyzed on SPSS for MacBook, 26.0

RESULTS

Patients in the FS group were older and showed relatively high frequencies of comorbidities including diabetes mellitus, hypertension, and coronary artery disease. A linear regression analysis of Ferritin against disease severity showed that ferritin was significant for disease severity (Adjusted R Square= 0.880). Ferritin was 105.70 ± 43.19 (ng/ml) for FM group and 725 ± 125.19 (ng/ml) for FS group

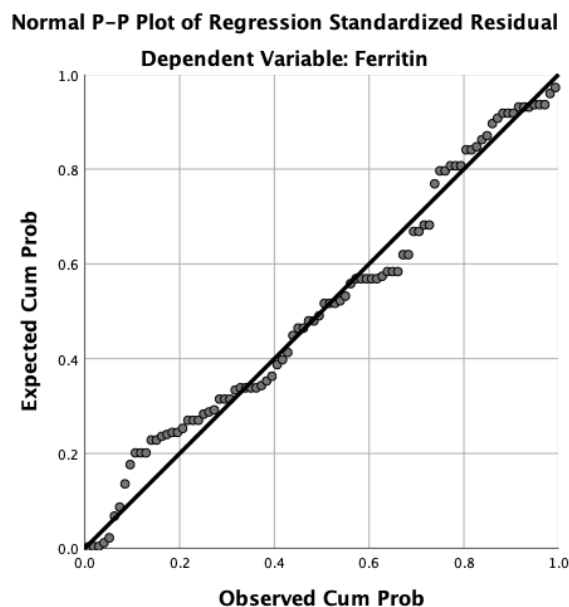


Fig. 1 Linear Regression Analysis showing the correlation of Ferritin against the severity of disease

Model Summary^b

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.939 ^a	.882	.880	76.27574

a. Predictors: (Constant), Severity

b. Dependent Variable: Ferritin

Fig. 2 showing the R values of the Linear Regression Analysis

FM Group (N=52)		FS Group (N=38)	
Parameter	Mean +/- SD	Parameter	Mean +/- SD
WBC (/cmm)	6100±47	WBC (/cmm)	9800±101
Ferritin (ng/ml)	105.70±25.19	Ferritin (ng/ml)	725 ±125.19
D-Dimers (ng/ml)	110±31	D-Dimers (ng/ml)	457±149
C-Reactive Protein (mg/dl)	4.33±1.03	C-Reactive Protein (mg/dl)	84.70±10.15

Fig. 3 Table showing biochemical parameters of the COVID-19 patients. (N=90)

Of the 38 patients in the FS group, 24 died and only 14 were discharged upon recovery. Whereas in the FM group all the patients were discharged upon recovery and none of the patients died due to covid related illness.

DISCUSSION

Our study found out that patients in the FS group were older and showed relatively high frequencies of comorbidities including diabetes mellitus, hypertension, and coronary artery disease. A linear regression analysis of Ferritin against disease severity showed that ferritin was significant for disease severity (Adjusted R Square= 0.880). Ferritin was 105.70±43.19 (ng/ml) for FM group and 725 ±125.19 (ng/ml) for FS group. Ferritin level was significantly higher in the severe group. In the biochemical parameters of the patient there was a significantly high count of white blood cells above the normal ranges.

COVID-19 is a deadly and fatal medical condition especially in elderly patients with comorbidities.⁸⁻⁹ A mean age range of 50 to 60 years is reported to be detrimental when it comes to comparing disease severity with age.¹⁰ It is reported in literature that old age patients had severe disease in comparison to younger patients.¹¹ This could also be explained by an increased frequency of comorbidities with ageing.

Studies have found out that patients with COVID-19 infection may present with elevated levels of Ferritin. Hyperferritinemia is now widely accepted and used by clinicians as an acute phase reactant to monitor disease progression and/or therapeutic response.¹² Our study found out significantly elevated levels of ferritin in the severe cases. Similarly, a study found out that elevated ferritin levels were observed in patients that did not survive.¹³

It is also important to note here that severe disease or those with elevated Ferritin levels showed high rates of death. A study reported a cut off value of >300 ng/mL with a higher death rate in those with a ferritin level greater than the cut off.¹⁴

The above-mentioned facts prompt us to believe hyperferritinemia to be a predictor of disease severity in COVID-19 patients and can be identified as an independent risk factor. Macrophage activating syndrome could be the possible explanation for the clinical course of severe illness, which is characterized by elevated ferritin levels and the presence of a cytokine storm. The H-chain of ferritin activating macrophages leads to an increased release of inflammatory cytokines in such patients.¹⁵

Our study has certain limitations. This was a single centered descriptive study with only a small sample size of 90 patients of mostly Pashtun ethnicity. The results can therefore not be generalized.

CONCLUSION

Ferritin levels might predict the disease severity effectively if done early on. Studies have shown that the levels of Serum Ferritin have been associated with mortality and morbidity. These need to be checked early on and taken as a marker of disease progression and recovery.

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