

Ferritin levels and COVID-19

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To the Editor,

Ferritin is a key mediator of immune dysregulation, especially under extreme hyperferritinemia, via direct immune-suppressive and pro-inflammatory effects, contributing to the cytokine storm¹. It has been reported that fatal outcomes by COVID-19 are accompanied by cytokine storm syndrome, thereby it has been suggested that disease severity is dependent of the cytokine storm syndrome². Many individuals with diabetes exhibit elevated serum ferritin levels³⁻⁵, and it is known that they face a higher probability to experience serious complications from COVID-19⁶. On this basis, we briefly review evidence supporting the hypothesis that ferritin levels might be a crucial factor influencing the severity of COVID-19.

In one study with 20 COVID-19 patients, it was found that individuals with severe and very severe COVID-19 exhibited increased serum ferritin level, being serum ferritin in the very severe COVID-19 group significantly higher than in the severe COVID-19 group (1006.16 ng/ml [IQR: 408.265-1988.25] vs 291.13 ng/ml [IQR: 102.1-648.42], respectively)⁷. In agreement with this, another study revealed that in patients who died by COVID-19, ferritin levels were high upon hospital admission and throughout the hospital stay. The median values of serum ferritin levels after day 16 of hospitalization exceeded the upper limit of detection in these patients, suggesting that ferritin levels increased non-stop⁸. Also, Chen et al. analyzed the clinical characteristics of 99 patients, in which 63 of them had serum ferritin way above of the normal range⁹. Elevated ferritin levels were

found also in autopsies of 12 patients whose cause of death was SARS-CoV-2 infection¹⁰. An analysis of the peripheral blood of 69 patients with severe COVID-19 revealed elevated levels of ferritin compared with patients with non-severe disease. Therefore, it was concluded that serum ferritin levels were closely related to the severity of COVID-19¹¹. Finally, 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 illness¹².

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 and is effective for long-term iron chelation therapy in beta-thalassemia and other maladies involving iron overload¹³. Manipulations decreasing dietary iron should be also considered as they have been shown to modify serum ferritin levels^{14,15}. Thus we hypothesized that this might reduce the exacerbation of COVID-19, specially in individuals with morbidities cursing with elevated ferritin levels such as diabetes³⁻⁵.

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