Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

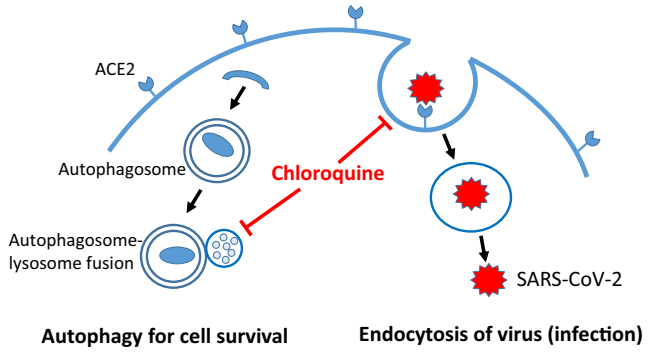

Figure 1 | Chloroquine could be a double-edged sword. Chloroquine may slow virus infection and replication early but may later potentiate tissue damage and worsen acute organ injury by inhibiting autophagy. ACE2, angiotensin-converting enzyme 2; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

impairing autophagosome-lysosome fusion and the degradative activity of the lysosome.[2] Also, chloroquine can induce an autophagy-independent severe disorganization of the Golgi and endosomal-lysosomal systems that may contribute to its effect on autophagosome-lysosome fusion.[2] Inhibition of autophagy by chloroquine results in the accumulation of damaged mitochondria due to the lack of clearance via mitophagy, which, together with attendant oxidative stress, leads to renal tubular dysfunction.[3] In patients, chloroquine increases cancer cell killing by inhibiting autophagy, an idea being tested in clinical trials.[4] In mouse models of septic AKI, autophagy protects against renal tubule injury and pharmacological inhibition of autophagy with chloroquine worsens kidney damage.[5] Chloroquine also blocks autophagic flux and worsens both ischemic and cisplatin-induced nephrotoxic AKI in mice.[6] Chloroquine has also been shown to be nephrotoxic by autophagy-dependent as well as autophagy-independent pathways, including interference with the cyclic adenosine monophosphate production and signaling in distal tubular cells.[7] In other preclinical studies, chloroquine inhibits autophagy and worsens ischemic cardiac injury[8] and sepsis-induced liver or lung injury.[9,10] Thus, chloroquine could be a double-edged sword: it may slow virus infection and replication early, but may later potentiate tissue damage and worsen acute organ injury by inhibiting autophagy (Figure 1). We write to strike a cautionary note on using chloroquine or hydroxychloroquine in COVID-19 patients with acute organ injury including AKI.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Figure S1. Angiotensin-converting enzyme 2 (ACE2) is the functional cellular receptor for SARS-CoV-2.

Supplementary References.

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Could ferritin help the screening for COVID-19 in hemodialysis patients?

To the editor: The screening for coronavirus disease 2019 (COVID-19) is challenging: many patients are asymptomatic, viral RNA detection in a nasopharyngeal swab is falsely negative in 30%, and a pulmonary computed tomography scan is useless in patients with no pulmonary involvement.[1,2]

In our hemodialysis center, following the Kidney Disease Improving Global Outcomes recommendations, ferritin levels are measured each month to detect iron deficiency.[3] In April 2020, there were 22 COVID-19 cases that had occurred within the 270 patients undergoing hemodialysis at our hemodialysis center. We noticed that ferritin levels were very high in these patients (Figure 1). When monthly ferritin levels were measured in April, 1 of our female patients had an unusually high ferritin level of 3806 ng/ml compared with 531 ng/ml previously. A clinical examination showed no clinical symptoms of COVID-19, but she was tested by nasopharyngeal swab and was shown to be positive.

We compared ferritin levels in patients undergoing hemodialysis who tested positive and negative for COVID-19 at our

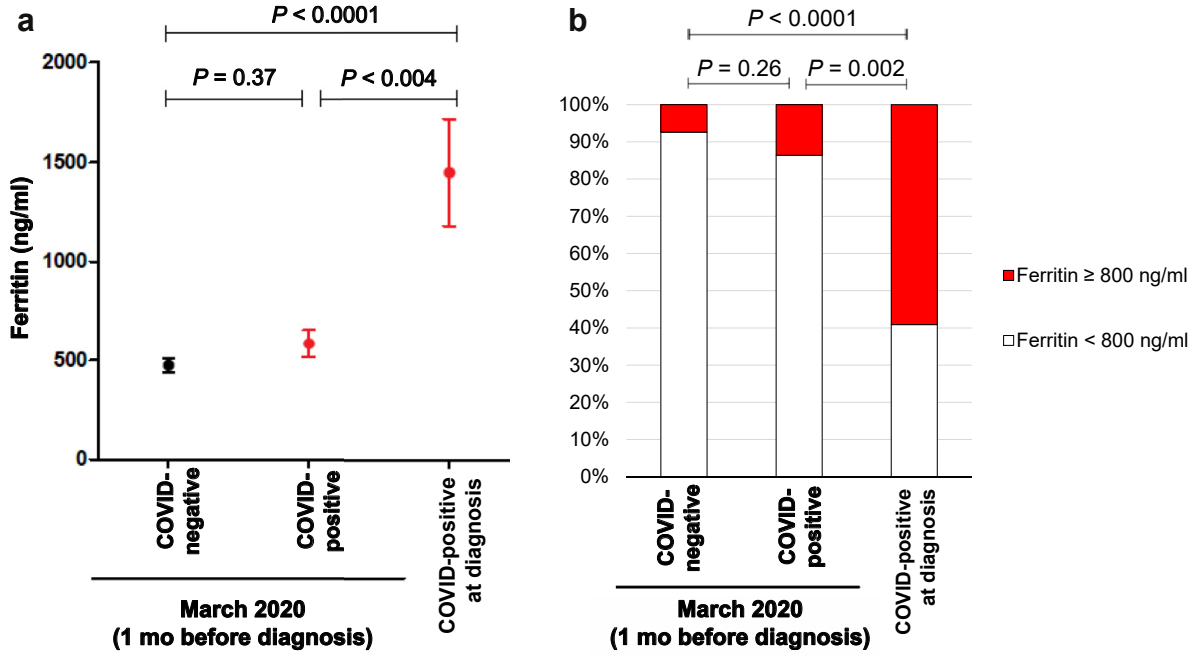

Figure 1 | Ferritin levels of coronavirus disease (COVID)–negative (n = 268) and COVID-positive (n = 22) patients receiving hemodialysis at our center prior to and at COVID diagnosis. (**a**) Comparison of ferritin levels during the first week of March 2020 (before the coronavirus disease 2019 [COVID-19] epidemic had occurred at our center) and at diagnosis of COVID-19 (Student *t* test). The first COVID-19 case in our center was diagnosed on March 18, 2020. (**b**) Rate of patients with ferritin levels greater than 800 ng/ml during the first week of March 2020 and at diagnosis of patients who tested negative and positive for COVID-19 (χ^2 test).

dialysis center in the month preceding viral infection and during infection and found a critical difference (Figure 1). In the patients who tested positive for COVID-19, the mean (±SD) ferritin levels in March (before viral infection) and at diagnosis were 584 ± 318 and 1446 ± 1261 ng/ml, respectively, which was a mean increase of 275%. Interestingly, ferritin levels were increased at diagnosis in the 5 asymptomatic patients as well as in the patients with symptoms (mean ± SD, 1209 ± 1292 and 1535 ± 1280 ng/ml, respectively). Ferritin levels remained stable or decreased very slowly during the whole period of sickness in almost all patients. The pathophysiological mechanisms underlying high ferritin levels have not been totally explained at this time, and some investigators have reported a cytokine storm syndrome or macrophage activation syndrome; however, in our cohort, ferritin levels were not correlated with C-reactive protein (data not shown).[4,5]

Screening for COVID-19 in hemodialysis centers is crucial so that infected patients can be isolated and to protect noninfected patients. Ferritin could be a helpful, available, and easy-to-use screening tool for the disease, although we believe that more research still is needed.

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De-isolation of COVID-19–positive hemodialysis patients in the outpatient setting: a single-center experience

To the editor: The advice for patients presenting with coronavirus disease 2019 (COVID-19) symptoms is to self-isolate for 7 days after the onset of symptoms for the individual case and