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.

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OPINION

Defective Anti-oxidant System: An Aggravating Factor for COVID-19 Patients Outcome?

Several comorbidities have been reported as risk factors for unfavorable prognosis in patients with COVID-19. The most common comorbidities that influence the outcome of COVID-19 patients are cardiovascular disease (CVD), diabetes mellitus type 2 (DMT2), hypertension, malignancy and chronic obstructive pulmonary disease (COPD) among others. Smoking has also emerged as a risk factor associated with a worse outcome. It has been shown that oxidative stress, a condition of imbalance between the release of reactive oxygen species (ROS) and the endogenous antioxidant capacity, is causally involved in the same diseases that increase the risk of a severe outcome from COVID-19, including CVD and DMT2 (1). It is also well-known that smoking can induce cellular oxidative stress while it depletes anti-oxidants through various mechanisms (2). Emerging evidence on COVID-19 indicates a male preponderance in both vulnerability and mortality. Based on data from China, the much higher smoking rate in men might explain the observation that COVID-19 poses a greater risk to men than women (3).

In terms of oxidative stress, dysregulation of glucose 6-phosphate dehydrogenase (G6PD) leads to increased oxidative stress and damage as this enzyme is responsible for generating NADPH, a key cellular reducing agent. Studies have shown that G6PD deficiency leads to increased sensitivity to even mild oxidative stress, while altered activity and levels of G6PD have been recognized as a marker of inflammation. Apart from the elevated oxidative stress, G6PD-deficient cells are at a greater risk for protein glycosylation (4), a process that plays an essential role in viral pathogenesis—including COVID-19— by promoting folding, trafficking and viral spread, whilst host cell and viral glycans are known to act as attachment factors (5,6). Notably, a previous study has shown that nicotine significantly inhibited G6PD activity in the rat lung, while the potent anti-oxidant vitamin E was able to restore this effect (7).

Could an intrinsically defective anti-oxidant system, such as G6PD deficiency or other causes, predispose to COVID-19 infection and poorer prognosis? To this end, Wu YH, et al. (8) demonstrated that human lung epithelial A549 cells with lower G6PD activity (via RNA interference) had a 12 fold higher viral production when infected with human coronavirus 229E, which shares a sequence similarity with COVID-19 and clinically resembles it, compared to control cells (8,9).

Considering all the above, is it rational to employ anti-oxidants in the fight against COVID-19? There is, so far, lack of evidence regarding the exact role of the anti-oxidant defense systems in COVID-19 infection. High dose supplementation with vitamins E and C or other anti-oxidants, when given at an early stage of the infection, may prevent the spread of the virus in the body providing protective effects and reducing severity of disease. In this vein, clinical studies with COVID-19 patients should be conducted taking also into account different ethnic/genetic backgrounds (e.g., geographic distribution of the X-linked G6PD deficiency). Currently, traditional medicine products and vitamins (such as SFJDC and vitamin C) that are involved in anti-oxidant defense systems are amongst the various additive treatments for COVID-19 under investigation according to World Health Organization (WHO) (10).

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Conflicts of Interest

The authors declare that there are no conflicts of interest.

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