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are present in olfactory epithelium. With the virus replicating in the nose and nasopharynx, this represents a mechanism for direct damage of olfactory epithelium by the virus in the frame of a mild infection.

In conclusion, the case presented in this report highlights the importance of urgent audiologic and radiologic diagnostics in COVID-19 patients who report hearing loss, especially if neurologic symptoms are present.

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Potential Competing Interests: The authors report no competing interests.

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<https://doi.org/10.1016/j.mayocp.2020.05.034>

Glucose-6-Phosphate Dehydrogenase Deficiency and COVID-19 Infection



To the Editor: One unsettling aspect of the coronavirus disease 2019 (COVID-19) (severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]) pandemic is the variable susceptibility to infection. Some people who

are exposed remain asymptomatic, others experience mild to moderate symptoms, while still others become severely ill and die. Hospitalization rates increase with age and approximately 90% of hospitalized patients have underlying medical conditions.¹ However, this does not account for a number of otherwise healthy or younger patients who are severely affected. Other suggested factors include genetic determinants.

A condition that should be considered is glucose-6-phosphate dehydrogenase (G6PD) deficiency. This X-linked recessive disorder with numerous allelic variants affects some 400 million people worldwide, with higher prevalence in Africa, the Mediterranean region, and Asia. Decreased production of G6PD results in deficient levels of nicotinamide adenine dinucleotide phosphate and reduced glutathione, causing oxidative stress and red blood cell destruction. Although frequently asymptomatic, patients may develop hemolytic anemia triggered by certain infectious agents and medications.² There is evidence to suggest an association between G6PD deficiency and increased susceptibility to, and severity of illness with, COVID-19 infection.

Wu et al³ found that G6PD deficiency enhanced infection of cells with human coronavirus 229E (HCoV 229E). Using G6PD-deficient fibroblasts and G6PD-knockdown cells derived from human lung epithelial cells subjected to viral inoculum in vitro, they found that viral gene expression was higher in these cells compared with control cells. Production of viral particles in the deficient cells was also higher over time, indicating that G6PD activity modulates this production. Further, the G6PD-deficient cells were more susceptible to HCoV 229E-mediated cell death. SARS-

CoV-2 may have a similar effect on cells in G6PD-deficient patients.

Spain and Italy have been particularly affected by the COVID-19 pandemic, with case fatality rates of 12.0% and 14.2%, respectively, as of this writing.⁴ G6PD deficiency is more common in the Mediterranean region. On the Italian island of Sardinia alone, the prevalence ranges from 10% to 15%.⁵ The allelic variants of G6PD deficiency in the Mediterranean region tend to manifest more significant phenotypic presentations. Although other factors may account for severity of illness in these countries, G6PD deficiency should be considered.

Reports from the United Kingdom and the United States show increased numbers of COVID-19 infection among members of minority groups. In the United Kingdom, 63% of the first 106 health care and social workers who died from the virus were black, Asian, or minority ethnic (BAME). BAME individuals make up 34% of patients admitted to UK intensive care units, although they only account for 17% of the population in the United Kingdom.⁶ In the United States, African Americans have been more significantly affected than other races. Yancy⁷ noted the infection rate in 131 predominantly black counties is 137.5 per 100,000 and the death rate is 6.3 per 100,000. These rates are three times and six times higher, respectively, than what are found in mostly white counties. Pre-existing medical conditions and adverse socioeconomic determinants of health may explain some of this disparity. However, G6PD deficiency is common among blacks and Asians. In a study of 63,302 US military personnel, 2.5% of males and 1.6% of females overall were deficient. Prevalence was higher among African American males (12.2%) and females (4.1%), as well as Asian males (4.3%).⁸

G6PD deficiency may play a role in COVID-19 severity of illness and death in these groups.

Vascular endothelial dysfunction and coagulopathy have been suggested as complications of COVID-19 based on a report of large vessel ischemic stroke occurring in five US patients under the age 50 years, including two without pre-existing conditions. Similar cases have occurred in China and Singapore.⁹ Coagulopathy has also been observed in people with G6PD deficiency. Albertsen et al¹⁰ reported a fatal hemolytic crisis with disseminated intravascular coagulation and pulmonary microthrombi in a 42-year-old G6PD-deficient African male. Hemolysis results in cell-free hemoglobin, which contributes to activation of the intrinsic coagulation cascade and clot formation. COVID-19 infection could be a trigger for hemolysis and coagulopathy in G6PD-deficient patients, thus explaining the stroke symptoms.

Chloroquine has infrequently been reported to cause hemolysis in G6PD-deficient patients and caution is advised for its use.¹¹ Hydroxychloroquine, its molecular variant, is generally considered safe. Both antimalarial drugs are being trialed as possible treatments for COVID-19. However, a recent report described an acute hemolytic episode occurring in a COVID-19 patient with G6PD deficiency who was treated with hydroxychloroquine.¹² Hydroxychloroquine may increase the oxidative stress in COVID-19 patients with G6PD deficiency, thereby serving as a trigger for hemolytic anemia.

Studies are needed to determine whether a positive correlation exists between G6PD deficiency and COVID-19, with respect to increased susceptibility to infection and severity of illness. This is important for several reasons. First, it will allow for

identification of a subset of COVID-19 patients for whom close monitoring and supportive care may be critical. Second, certain treatments, such as hydroxychloroquine, may be contraindicated in these patients. Third, identification of this relationship may suggest other therapies, such as use of antioxidants, that may prove beneficial for treating COVID-19. Finally, such information will be important for people with known G6PD deficiency to guide their decisions and actions to prevent COVID-19 infection.

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<https://doi.org/10.1016/j.mayocp.2020.05.035>

Vitamin D Supplementation During the COVID-19 Pandemic



To the Editor: The coronavirus disease 2019 (COVID-19) pandemic has severe short-term and long-term consequences on individuals, health systems, and economies. Considering the studies on the role of vitamin D in the prevention of acute respiratory infections, supplementation of vitamin D may be reasonable also for the prevention of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections and reducing morbidity and mortality in COVID-19 high-risk patients.

Vitamin D deficiency is more common in older age groups, smokers, those who are obese, and in patients with chronic diseases such as diabetes, hypertension, various gastroenterological diseases, and also in African Americans.¹ The