The possible role of glucose-6-phosphate dehydrogenase deficiency in COVID-19 global prevalence and distribution

Sir,

The new coronavirus 2019 (nCoV-19), also known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first reported on December 2019 and began an outbreak known as a pandemic declared by the World Health Organization (WHO). Given the rapid spread of coronavirus disease 2019 (COVID-19) worldwide, morbidity and mortality rate is increasing rapidly every day. nCoV-19 is a novel species of positive-sense, single-stranded RNA of Coronaviridae family categorized as beta coronaviruses subfamily along with SARS-CoV and Middle East respiratory syndrome coronavirus.[1]

Conventional cellular metabolism produces a wide range of reactive oxygen and nitrogen species (RONS) byproducts. The reactive oxygen species production following virus entrance into the host cells leads to the activation of oxidative pathways and ultimately oxidative burst, which is due to imbalance of production/scavenging RONS. The oxidative burst subsequently induces apoptosis or necrotic cell death. Based on previous researches, many retroviruses, DNA and RNA viruses, can induce apoptosis by generating oxidative stress in infected cells.[2]

One of the most important enzymes in the redox biology conservation is glucose-6-phosphate dehydrogenase (G6PD), which acts through reduction of nicotinamide adenine dinucleotide phosphate (NADP) to reduced form of NADP (NADPH) and regeneration of reduced glutathione (GSH). GSH is considered as the most abundant and vital endogenous antioxidant that protects cells against oxidative or nitrosative damage.[3]

Based on the application of models with disturbed redox balance, G6PD seems to play an important antiviral role in the body. The critical value of a redox milieu in coxsackievirus, rhinovirus, and influenza virus is now well documented with administration of antioxidant-rich diet containing glutathione, Vitamin E, and selenium. Moreover, there is enough evidence, indicating that G6PD status is determinative for enterovirus and coronavirus infection outcome and G6PD deficiency leads to increased cytopathic effect and the number of progeny release. Thus, G6PD deficiency renders a wide range of cells more susceptible to oxidative stress consequences.[4]

G6PD deficiency is known as the most common inherited human enzyme deficiency worldwide. Its prevalence in Iran is 6.7% (men: 8.8% and women: 2.2%) with the highest prevalence in Mazandaran province (13.6%) and the lowest in Mashhad city (0.8%) located in North and Northeast of Iran, respectively. The outbreak of COVID-19 in Iran reported to be the highest in the north part including Mazandaran, Gilan, and Golestan provinces, with the concomitant highest prevalence of G6PD deficiency in Iran.[5]

Furthermore, based on recent studies, the COVID-19 morbidity and particularly mortality rate is higher in men than in women.[6,7] One of the possible explanations for the higher prevalence of COVID-19 in male population might be considered the X-linked inheritance pattern of G6PD in human population, higher rate of G6PD deficiency in men, and subsequent altered redox homeostasis.[8]

The same condition exists in Italy with the high prevalence of G6PD deficiency among European countries, which is accompanied with a reduced antioxidant capacity as compared with normal individuals.[8] Thus, it could be predicted that COVID-19 would probably be associated with more morbidity and mortality rate in malaria-ridden nations including Sub-Saharan African countries in Southern Hemisphere with the greatest G6PD deficiency prevalence in near future with starting the cold weather similar to what happened in Iran and Italy.

It could be concluded that consumption of supplements and ingredients with high antioxidant capacity including Vitamin E, selenium, glutathione, and flavonoids might be beneficial in COVID-19 patients due to providing and maintenance of a redox milieu and deteriorating the host cell predisposition to nCoV-19 infection consequences. In addition, prescription of drugs including nitrofurans, quinolones, sulfonamides, aspirin, Vitamin C, and streptomycin is better to be prohibited due to high oxidative capacity.

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Conflicts of interest

There are no conflicts of interest.

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