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THE ROLE OF HEMOGLOBINOPATHY IN COVID-19 PATHOLOGY

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ABSTRACT
The novel coronavirus (Covid-19) is spreading rapidly worldwide. According to the World Health Organization, about 5.300 million people have been infected up to now and more than 340000 were died from Covid-19 infection (WHO, 2020). Every day, more and more unknown aspects of this "mysterious virus" are presented to researchers and clinicians. Based on available studies, the main pathology of the disease is that the coronavirus enters the cell by binding to ACE2 receptors and leads to proliferation and destruction of respiratory tract cells and pneumonia (Ge et al., 2013). Findings about the pathology of the disease are low and mostly have been stated based on assumptions. At the beginning of the disease prevalence, it was believed that the virus only involved the respiratory tract, leading to severe pneumonia and hypoxia, and finally death. However, recent reports suggest that in addition to the lungs, other organs, such as the heart, kidneys, eyes, and digestive tract, are also affected (Yuen et al., 2020). These findings have led to a revision of the pathology of the disease, and researchers are investigating new dimensions effects of the virus.

Based on previous findings about SARS and other viruses that infect the respiratory systemchanging hemoglobin values may be a predictive factor of worsening clinical progression in patients with Covid-19 because of significantly reduced hemoglobin values in these patients as well other types of pneumonia (Lippi & Mattiuzzi., 2019). Data from Liu and Li (2020) suggest that the virus attacks 1-Beta chain of hemoglobin, dissociating it from iron to form porphyrin so that less and less hemoglobin will be available to carry oxygen and carbon dioxide. Although theproposals of Liu and Li have been seriously queried by Read (2020) the implications of their hypothesis should be considered in some detail. It seems to us that destruction of hemoglobin may be one of the key roles played by the virus, because of the impairment oxygen delivery to vital organs such as the brain, heart, kidneys and liver. Given that the death rate of elderly patients succumbing to the virus is very high and that anemia is relatively common among those over 60 years (Lanier et al, 2018), further diminution of oxygenationto the organs may well explain the increased mortality. As we know, in many deaths caused by Covid-19 virus, tachycardiafirst occurred, followed by a fatal heart attack. It seems that after binding virus withhemoglobin, releasing ions lead to release free radicals which increase oxidative activity in the organs, leading to further hypoxia (Faiqet al., 2020). Many patients, who recovered and were discharged, still complained of shortness of breath and fatigue although their lungs were completely cleared of the virus (Ahmad et al., 2020).

Normally, hemoglobin delivers oxygen from the lungs and delivers it into tissues and organs. Each hemoglobin molecule contains four heme molecules, each of which binds specifically to oxygen in the lungs, during chemical interactions. The ions of iron (Fe2+or Fe3+) which are part of the structure of oxyhemoglobinare toxic in the free state and will increase blood oxidative stress (Emerit et al, 2001, Lippi et al., 2019). Assuming that the corona virus attaches to hemoglobin, FE++ or FE+++may be released into the blood and tissues, and this is where the main effects of the virus begin. In this case, the function of hemoglobin is impaired and the oxygenation process is diminished and corporeal hypoxia will constantly increase (Buoro & Lippi., 2018), perhaps explaining the shortness of breath and fatigue following recovery in some patients (Zhou et al., 2020). Decreased blood hemoglobin with elevated serum ferritin, erythrocyte sedimentation rate, C-reactive protein, albumin, and lactate dehydrogenase also low oxygen saturation may be evidence of this hypothesis. Patients'

low oxygen saturation even when a ventilator is employed is further evidence (Faiqet al., 2020, Lippi & Mattiuzzi., 2019, Chen et al., 2020). The other reason for this assumption is that based on the study by Lansiauxet al., 2020, which indicates that beta-thalassemia subjects are immunized against Covid-19. Beta-thalassemia results of a default in the hemoglobin beta- chain synthesis, indicating that Covid-19 attacks beta chain of hemoglobin.

It may be that the main reason for the appearance of patchy consolidation and ground glass opacities in the lungs (Kong and Agarwal, 2020, in press) is due to tissue damage caused by the presence of these free ions and consequently free radicals. The epithelial surface of alveoli containshigh volumes of antioxidant molecules such as nuclear factor-erythroid 2 related factor 2 (Nrf2) (Kosmider et al., 2012), but these may not be sufficient to counteract those derived from damaged hemoglobin.

In patients suffering from Covid-19, we would recommend that oxidative stress indicators and the amount of antioxidant enzymes and oxidative products in these patients be evaluated.

Blood transfusions or sera transfusions may need to be performed regularly in such patients while maintaining them with hyperbaric oxygen.

Author contributions

RF, ASJ and WW conceived and designed, read and approved the submitted version of the study, RF wrote the preliminary manuscript, WW and ASJ contributed to its technical revision.

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Conflicts of interest

The authors declare no conflicts of interest.

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