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## Long COVID-19 laboratory findings in hemodialysis patients: Should they be considered post-COVID syndrome?

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The increasing number of patients who have recovered from COVID-19 and the growing data regarding the long-term symptoms of the disease require further research. In this letter, we focused on laboratory manifestations following COVID-19 recovery in hemodialysis patients, a subject that has not yet been studied. We identified a high prevalence and diversity of changes in the laboratory values in clinically stable or asymptomatic COVID-19 patients who were on hemodialysis. We believe that the issues discussed here would be reflected in further research to clarify whether these laboratory changes in post-COVID-19 asymptomatic hemodialysis patients should be added to the definition of post-COVID syndrome.

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**Dear Editor,**

Currently, the world is under pressure from the novel coronavirus-19 (COVID-19) disease, which is caused by severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2). COVID-19 has caused more than five million confirmed deaths globally (1). The greatest risk of morbidity and mortality from COVID-19 is in older people, diabetics, and patients with immune dysfunction or chronic cardiovascular or kidney diseases (2). Hemodialysis (HD) is the most common modality of dialysis kidney replacement therapy worldwide (3,4). Patients treated with HD are at high risk for adverse outcomes of COVID-19 because a significant number of them are elderly and have a high prevalence of comorbidities (3-5), which not only increases the risk of infection with COVID-19 but also the formation of life-threatening complications (6,7). It has been demonstrated that the clinical symptoms of COVID-19, such as fever, pneumonia, and cough, are less common in HD patients than in the general population who infected with COVID-19, and even though about 25% of them have asymptomatic cases (6,7). However, the mortality rate from COVID-19 in HD patients is more than 30%,

which is 20 times higher than in the general population (6-8).

People who survive COVID-19 may still exhibit one or more symptoms in the post-acute phase of the disease (2,9). This status is called post-COVID-19 syndrome, which is defined as persistent signs and/or symptoms of COVID-19 that last for more than four weeks from the onset of the disease and are not linked to alternative diagnoses (9,10). These post-COVID-19 symptoms are highly varied, but the most commonly reported ones are cognitive impairment; sleep disturbances; breathlessness; cough; low-grade fever; chest, abdominal and muscle pain; and also fatigue (8-10). Similar to the general population, HD patients experience the symptoms persistently and exhibit an increased risk of mortality six months after recovery (10). However, data on the long-term outcomes of COVID-19 in HD patients are limited and remain unclear. To the best of our knowledge, there is the only published study on this topic in HD patients conducted by Och et al (10). In this study, the authors demonstrated that 81% of HD patients experienced one or more post-COVID-19 symptoms six months after recovery (10). It should be emphasized that the majority of published data

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on this topic are based on self-reported symptoms, while only a few studies have included an assessment of the laboratory data of COVID-19-recovered patients (11,12). In particular, Varghese et al observed lymphopenia in 14% of COVID-19 patients, even beyond a 90-day follow-up (11). In addition, the authors demonstrated that about 10% of the patients had increased values for creatine kinase, glucose, potassium, low-density cholesterol, and platelet counts (18). Mohiuddin Chowdhury et al found post-COVID leukocytosis (16.1%), lymphocytosis (14.5%), and an increased prothrombin time (25.8%) in a relatively young cohort of COVID-19 patients (12).

Our multicenter observations during a mean follow-up period of 12 months found that the prevalence of post-COVID-19 self-reported symptoms in HD patients was significantly lower than in the general population whereas almost all of them (98%) had certain changes in routine blood tests. Apart from the classic biomarkers of the ongoing inflammatory cascade and the adverse outcomes of COVID-19, such as lymphopenia and increased values for D-dimer, serum ferritin, and C-reactive protein, we identified impaired hemostatic balance, dysglycemia, hyperkalemia, an abrupt decrease in the levels of hemoglobin, calcium, and high-density lipoprotein, and the formation of atherogenic dyslipidemia, even in patients who were clinically stable and asymptomatic for COVID-19 (Figure 1). Furthermore, we often observed conflicting changes in the serum concentrations of phosphate and parathyroid hormone in HD patients who had previously exhibited concentrations within the reference range. Specifically, in some HD patients who had recovered from COVID-19, the values for phosphate and parathyroid hormone increased significantly, while those values decreased substantially in others. Frequently, the findings of such blood tests were the only reason for

the testing for COVID-19. Interestingly, the likelihood of developing these laboratory abnormalities was not associated with the severity of the COVID-19 infection or the presence of clinical symptoms following recovery. Logically, the incredibly high prevalence of adverse laboratory findings in HD patients who had recovered from COVID-19 is associated with end-stage kidney disease and high comorbidity. However, the presence of these laboratory abnormalities in HD patients following asymptomatic cases of COVID-19 is still far from understood.

Accordingly, our findings support the presence of a common set of laboratory abnormalities in the vast majority of HD patients who have recovered from COVID-19, regardless of the severity of the disease. Therefore, we believe that not only the persistence of one or more clinical symptoms but also the changes in laboratory values following recovery from COVID-19 should be included in the definition of post-COVID syndrome for HD patients. Finally, we expect that our observations will be reflected in future research to clarify the interaction mechanisms and prevent morbidity and mortality in HD patients who have had COVID-19.

#### Authors' contribution

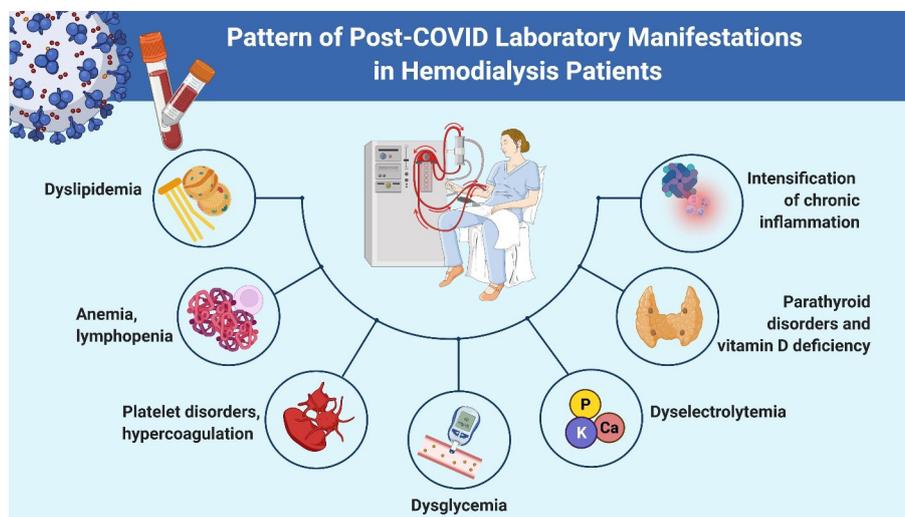
Both authors (NS & AR) made substantial contributions to conceptualizing and designing the manuscript. NS is the corresponding author. They both have approved its current version for publication.

#### Conflicts of interest

The authors declare no conflicts of interest in this paper.

#### Ethical issues

This letter to the editor was conducted in accord with the



**Figure 1.** Post-COVID laboratory manifestations in HD patients (created with BioRender.com).

World Medical Association and Declaration of Helsinki. Ethical issues including plagiarism, double publication and redundancy have been completely observed by the authors.

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