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LETTERS TO THE EDITORS

Is insulin resistance truly responsible for post-COVID depression?

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We read with interest the article by Al-Hakemi et al. on a retrospective cohort study of 86 patients with long-COVID syndrome that investigated the relation between post-COVID depression and insulin resistance.[1] Depression was assessed with the Beck Depression Inventory and the Hamilton Depression Rating Scale, while insulin resistance was assessed with the Homeostasis Model Assessment 2 Calculator.[1] It was found that one third of the post-COVID patients had insulin resistance, increased fasting glucose, or increased insulin levels.[1] Insulin resistance was associated with depressive symptoms.[1] The study is excellent, but its limitations are a cause for concern and should be discussed.

One such limitation is that no HbA1c values were measured in any of the long-COVID-19 patients. Knowing the HbA1c values is crucial for determining whether the patients had pre-diabetes or diabetes.

Another limitation is that C-peptide levels were not measured instead of insulin. Serum C-peptide levels are independent of both exogenous insulin application and the amount of insulin antibodies. A similar limitation is that no insulin antibodies were measured.

We disagree with the notion that post-COVID syndrome is the same as long-COVID syndrome. Post-COVID is defined as symptoms lasting a maximum of 12 weeks, whereas the symptoms in long-COVID syndrome last $>$ 12 weeks.

One argument against insulin resistance as the cause of post-COVID depression is that it has not been previously reported. A second argument against causality is the small size of the investigated cohort (n=86). The strongest argument against causality, however, is that alternative causes of depression were not reported. We should have been informed of the other symptoms or signs found in the post-COVID group. Because post-COVID is commonly associated with "brain fog," headache, impaired cognitive function, impaired concentration, insomnia, nausea, vomiting, stomach pain, diarrhea, fatigue, myalgia, irritable bowel syndrome, and muscle weakness,[2] it is crucial to know which of these manifestations could have contributed to depressive symptoms.

Because COVID-19 can be complicated by pancreatitis,[3] it is critical to determine how many patients had abdominal pain, elevated amylase or lipase, or abdominal ultrasound indicative of pancreatitis. Pancreatitis may be complicated by reduced insulin levels and diabetes.

Because about half of the patients with post-COVID syndrome had metabolic syndrome, and most patients with metabolic syndrome have insulin resistance,[4] it is conceivable that insulin resistance was not associated with COVID-19 but rather with pre-existing metabolic syndrome. In the 45 patients diagnosed with metabolic syndrome, it should have been determined whether the condition was present prior to SARS-CoV-2 infection.

Overall, this interesting study has limitations that call the results and their interpretation into question. Addressing these issues would strengthen the study's conclusions and could improve its status. Before attributing depression in post-COVID syndrome to insulin resistance, alternative causes of depression must be thoroughly ruled out.

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Disclosure

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References

1 Al-Hakeim HK, Al-Rubaye HT, Jubran AS, Almulla AF, Moustafa SR, Maes M. Increased insulin resistance due to Long COVID is associated with depressive symptoms and partly predicted by the inflammatory response during acute infection. Braz J Psychiatry. 2023;45:205-15.
2 Yan MZ, Yang M, Lai CL. Post-COVID-19 syndrome comprehensive assessment: from clinical diagnosis to imaging and biochemical-guided diagnosis and management. Viruses. 2023;15:533.
3 Hatami D, Alavi SMA. Complicated appendicitis, acute pancreatitis, pleural effusion, and sinus bradycardia in a COVID-19 patient. Clin Case Rep. 2023;11:e7077.
4 Roberts CK, Hevener AL, Barnard RJ. Metabolic syndrome and insulin resistance: underlying causes and modification by exercise training. Compr Physiol. 2013;3:1-58.