Insulin resistance as a common clinical feature in diabetes mellitus, obesity, hypertension, dyslipidemia, and atherosclerosis deserves more attention in COVID-19

Dear Editor,

COVID-19 has evolved into a worldwide crisis, and the WHO has declared its outbreak a Public Health Emergency of International Concern. Diabetes mellitus, obesity, hypertension, dyslipidemia, and atherosclerosis are well-known comorbidities that adversely influence the outcome in COVID-19 patients, and insulin resistance, as a shared risk factor for these metabolic disorders, can be of particular importance in the pandemic.[1] Based on reports, among comorbidities associated with COVID-19, the highest mortality rates are related to cardiovascular disease and diabetes mellitus.[2] Insulin resistance is involved in the development of both these diseases. Insulin resistance and cardiovascular disease boost the inflammatory state, which may lead to increased severity of COVID-19. Furthermore, diabetes mellitus, cardiovascular disease, and kidney disease (diseases associated with insulin resistance) are comorbidities shown to contribute to increased vulnerability to pneumonia-associated organ failure.[2]

It appears that angiotensin-converting enzyme 2 (ACE2), the cellular receptor of SARS-CoV-2, plays an important role in the relationship between COVID-19 severity and insulin resistance. Type 2 diabetes was found to be causally associated with increased expression of ACE2 in the lung. Elevated ACE2 expression due to diabetes and related traits may affect the risk of COVID-19 and exacerbate its complications.[3] In addition, soluble ACE2 levels have significant associations with all metabolic syndrome components, including insulin resistance, obesity, hypertension, and hyperlipidemia.[4]

Increased cytokine levels and hypokalemia, which occur in patients with COVID-19, could increase insulin resistance. Serum concentrations of C-reactive protein, ferritin, and alanine aminotransferase, biomarkers found to increase in COVID-19 patients, have also been associated with insulin resistance.[5] Furthermore, the assessment of serum fetuin-A, a glycoprotein involved in impaired insulin resistance, should be considered in SARS-CoV-2 infection as it was found to increase in SARS-CoV infection[5] [Figure 1]. Elevated reporting of insulin resistance in patients with COVID-19 can help advance our understanding of the metabolic aspects of this disease. Notably, the methods such as the homeostasis model of insulin resistance (HOMA-IR) and the quantitative insulin sensitivity check index (QUICKI), which use fasting glucose and insulin, are easily assayed by inexpensive blood tests.

While researchers and clinicians have focused on the acute phase of COVID-19, we may be unaware of the lasting consequences of this unknown disease. Hence, the continued monitoring of long-lasting consequents can be considered. Insulin resistance may be used as a marker for monitoring the possibility of developing diabetes mellitus in the future in COVID-19 patients who have recovered from the disease. Importantly, it should be noted that adverse metabolic effects of SARS-CoV-2 infection may be persistent without specific clinical symptoms. These avenues of research warrant attention and substantiation in large prospective cohort studies.

The SARS-CoV-2 infection has been associated with several metabolic disorders. It appears that COVID-19 patients with these disorders may have a
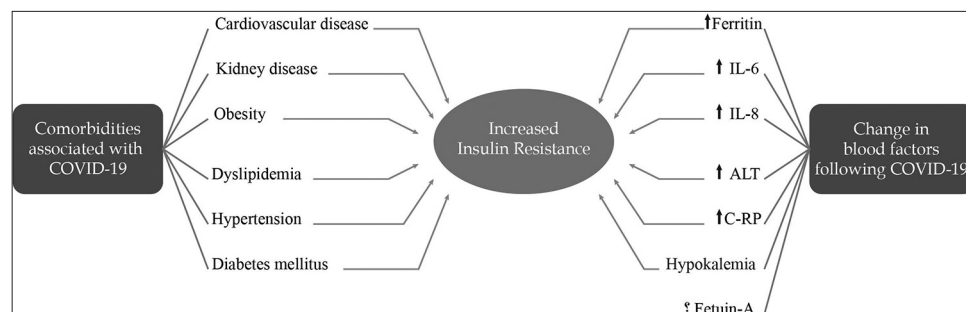

Figure 1: Comorbidities associated with COVID-19 can lead to increased insulin resistance, and altered blood factors following COVID-19 such as elevated ferritin and C-RP and hypokalemia have been associated with insulin resistance

higher risk of severe condition and mortality. Furthermore, patients with severe COVID-19 could develop high degrees of insulin resistance. These findings highlight the need to investigate insulin resistance as a common factor of the metabolic disorders and explore the possibility of using this factor in the overall assessment of the status of metabolic complications in patients afflicted by COVID-19. Insulin resistance should be considered as a candidate factor in the process of monitoring the long-term metabolic consequences of the COVID-19 infection. It is notable that some medications used in COVID-19 therapy contribute to the improvement of insulin sensitivity and the increase in insulin secretion. Daily supplementation with green tea may have several favorable metabolic and cardiovascular effects, including improvement of blood pressure, insulin resistance, inflammation, and oxidative stress, and lipid profile.[6] Medical and health-care professionals need to be aware of the importance of insulin resistance in assessing the metabolic profile, particularly in the management of COVID-19, a complex disease that has posed a global health challenge.

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Conflicts of interest

There are no conflicts of interest.

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