Stress Hyperglycemia Ratio may Portend Poor Outcomes in COVID-19

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Dear Editor,

Amidst an ardent interest in the pathophysiological and prognostic links between diabetes mellitus and coronavirus disease-2019 (COVID-19), the concept of stress hyperglycemia merits concurrent research attention. This becomes particularly relevant in the background of reports of an augmented disease severity in COVID-19 patients demonstrating elevated admission blood glucose levels, irrespective of the preexisting diabetic status.[1,2]

The absolute degree of admission hyperglycemia has been described to be associated with poor COVID-19 outcomes by Lazarus et al. (33% increase in the risk of severe disease for every 1 mmol/L rise in the admission fasting blood glucose) in their dose-response meta-analysis.[1] Moreover, few independent researchers outline a worsened attributable prognosis (owing to admission hyperglycemia) in nondiabetics ahead of the diabetics.[2]

While hyperglycemia at presentation emerges as a pertinent prognostic finding, the findings of a French nationwide multicenter CORONADO study [severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and diabetes outcomes] simultaneously undermine the isolated prognostic implications of the background glycemic control [assessed by glycated hemoglobin (HbA1c)].[3] This highlights the outcome predictive significance of acute hyperglycemia over and above the chronic glycemic control, particularly in the absence of long-term adaptations to deal with the hyperglycemia-exacerbated constellation of endotheliitis, oxidative stress, and thrombosis (well-known features of a severe COVID-19 infection, inflammation being the common denominator).[4]

In this context, stress hyperglycemia ratio (SHR), introduced by Roberts et al., is computed as the ratio of admission blood glucose and the estimated average blood glucose derived from HbA1c, thereby adjusting for the background glycemia adequately. Withstanding this fact, SHR can potentially be a superior marker of the relative extent of the stress glycemic response to the intercurrent critical illnesses, such as an underlying COVID-19 infection.[5] The findings of Fabbri et al., revealing a significantly accentuated mortality prediction with an odds ratio of 5.25 and area under the receiver-operating characteristic curve of 0.864 attributable to a SHR $\geq$1.14 in critically ill septic diabetics, bear testimony to the same.[5] In addition, independent research groups also emphasize the importance of disease-related glycemic alterations in contemplating risk stratification of the critically ill based on their depiction of an improved inhospital mortality prediction with the inclusion of the component of stress-induced hyperglycemia to the Acute Physiology and Chronic Health Evaluation (APACHE II) score.[5]

Therefore, premised on the aforementioned discussion, future research endeavors focusing on the concept of relative hyperglycemia are advocated wherein an elevated SHR may portend poor outcomes in the setting of COVID-19.

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