

What is the role of admission HbA1c in managing COVID-19 patients?

To the Editor,

Some recent articles published in the *Journal of Diabetes* have raised concerns about the importance of checking glycosylated hemoglobin (HbA1c) upon hospital admission for coronavirus disease 2019 (COVID-19) patients.¹⁻³ It is now undoubtedly clear that absolute hyperglycemia at the time of admission increases the risk of severe outcomes of COVID-19, independent of prior diabetes status,^{4,5} and tight glycemic control improves the prognosis of these patients significantly.^{4,5} However, the role of

admission HbA1c, which reflects average glycemia over the preceding 2 to 3 months, in the management of COVID-19 patients remains uncertain.

Some studies have shown a significant association between admission HbA1c and disease progression or mortality in COVID-19 patients, whereas a few others did not (Table 1). While the reasons for this discrepancy are not clear, most of these studies are constrained by a small number of patients,^{6,7} a large proportion of missing HbA1c data,⁸ and inadequate adjustment of potential

TABLE 1 Admission HbA1c and clinical outcomes in COVID-19 patients

Authors and country	N	Known diabetes, n (%)	Mean (SD) or median (IQR) HbA1c (%)	Outcome (s)	Findings	Variables adjusted for
Liu L et al, ⁷ China	77	33 (43.0)	NR	Mortality	1% increase in HbA1c was significantly associated with mortality with an hazard ratio of 1.58 (95% CI 1.16, 2.15), <i>P</i> = .004	Age, lactate dehydrogenase, lymphocyte count, NT-proBNP, and serum ferritin
Liu Z et al, ⁶ China	64	64 (100)	8.1 (6.6-9.7)	Disease progression (transferred to ICU or death) during hospitalization	1% increase in HbA1c was significantly associated with disease progression with an OR of 3.29 (95% CI 1.19, 9.13), <i>P</i> = .022	Maximum of in-hospital blood glucose, lymphocytes, CRP, and prothrombin time
Wang Z et al, ⁹ China	132	31 (23.5)	6.4 (5.8-7.2)	Mortality Markers of inflammation and hypercoagulability, and oxygen saturation	Higher mortality rate with increasing HbA1c levels: 9.8% in group A (n = 41, no diabetes and HbA1c ≤6.0%), 11.4% in group B (n = 44, no diabetes and HbA1c >6.0- < 6.5%), and 27.7% in group C (n = 47, diabetes and/or HbA1c ≥6.5%), <i>P</i> = .04 Negative correlation between HbA1c and SaO ₂ (r = -0.22,	None

(Continues)

TABLE 1 (Continued)

Authors and country	Known diabetes, n (%)	Mean (SD) or median (IQR) HbA1c (%)	Outcome (s)	Findings	Variables adjusted for
				$P = .01$). Positive correlation between HbA1c and ferritin ($r = 0.24$, $P = .01$), CRP ($r = 0.22$, $P = .01$), fibrinogen ($r = 0.27$, $P < .01$), and ESR ($r = 0.27$, $P < .01$)	
Cariou B et al, ⁸ France	1317 1317 (100)	8.1 (1.9)	Invasive mechanical ventilation or death within 7 days of admission	No significant association: compared with HbA1c <7%, OR for 7%-7.9% was 0.84 (95% CI 0.55, 1.27), OR for 8%-8.9% was 0.92 (95% CI 0.59, 1.45), and OR for $\geq 9.0\%$ was 0.78 (95% CI 0.51, 1.21)	None
Ling P et al, ¹ China	51 51 (100)	8.0 (1.5)	Disease progression (nonsevere to severe illness)	No significant association	Age, sex, blood glucose, smoking status, and blood pressure

Abbreviations: CI, confidence interval; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; HbA1c, glycosylated hemoglobin; ICU, intensive care unit; IQR, interquartile range; NR, not reported; NT-proBNP, N-terminal prohormone natriuretic peptide; OR, odds ratio; SaO₂, oxygen saturation; SD, standard deviation.

confounders.^{8,9} Previous research has shown that background glycemia mediates the association between admission glucose and outcomes in patients with a variety of medical conditions.¹⁰⁻¹² Thus, correcting admission glucose levels for background glycemia estimated by HbA1c, the so-called relative hyperglycemia predicts outcomes in acute health conditions better than absolute hyperglycemia,^{10,13} albeit not yet proven in the COVID-19 context.

Since HbA1c is relatively unaffected by the stress of acute illness,¹⁴ it may help identify newly diagnosed diabetes cases in COVID-19 patients. Newly diagnosed diabetes (new onset or previously undiagnosed) is now increasingly recognized as a common phenomenon in COVID-19 patients.^{15,16} More importantly, COVID-19 patients with newly diagnosed diabetes appear to be at a greater risk for poor prognosis not only compared with those without diabetes but also individuals with known diabetes.¹⁷⁻¹⁹

To summarize, admission blood glucose is certainly a key biomarker to risk stratify and guide the clinical management of COVID-19 patients, with or without known diabetes. Thus, it is essential that all COVID-19 patients be screened for absolute hyperglycemia upon admission so that early and appropriate treatment can be initiated if required. While the role of admission HbA1c as a marker


of COVID-19 severity is yet to be fully established, HbA1c assists in identifying patients with newly diagnosed diabetes.^{15,20} These patients are a high-risk group and should be closely monitored for the emergence of cardiometabolic disorders in the long term.¹⁶

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