




Comment On: “Association Between the Hemoglobin Glycation Index (HGI) and Risk of Diabetic Nephropathy: A Retrospective Cohort Study” [Letter]

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Dear editor

The retrospective cohort study by Zhou et al on the association between the Hemoglobin Glycation Index (HGI) and the risk of Diabetic Nephropathy (DN) in patients with Type 2 Diabetes Mellitus (T2DM) is the first to reveal a significant U-shaped relationship between the two, offering a novel biomarker and clinical perspective for early risk assessment of DN. This work holds considerable theoretical significance and potential clinical application value.¹ While the study provides an in-depth exploration of the underlying mechanisms, several critical issues regarding its applicability in real-world clinical settings warrant further investigation to enhance the translational potential and practical utility of these findings.

First, the study did not systematically examine potential interactions between HGI and different glucose-lowering treatment regimens. In clinical practice, management strategies for T2DM patients are highly individualized, involving subcutaneous insulin, oral hypoglycemic agents, and combination therapies. These treatments vary in their effects on glycemic variability and the hemoglobin glycation process.² For instance, insulin therapy may lead to more frequent hypoglycemic episodes, and the metabolic stress induced by glucose insufficiency can significantly affect erythrocyte properties,³ thereby altering the correlation between HbA1c and actual blood glucose levels. Therefore, further analysis of the predictive performance of HGI for DN risk across different treatment subgroups could help identify which patient populations would benefit most from HGI monitoring, thus enabling more targeted and individualized DN risk stratification and surveillance strategies for clinicians.

Second, the clinical operability of HGI remains to be clarified. Although the linear regression model developed in the study—based on fasting blood glucose and HbA1c—performed well within the cohort, its generalizability across diverse ethnicities, age groups, and comorbid conditions has not been validated. For example, hypertensive patients often present with microvascular complications,⁴ and HbA1c levels are closely related to peripheral microvascular damage in diabetic patients.⁵ Should the HGI threshold be adjusted for diabetic patients with comorbid hypertension?

Future research should employ multicenter, prospective designs incorporating more comprehensive clinical variables and treatment information to further evaluate the performance of HGI across different therapeutic strategies and population subgroups. Efforts should also focus on developing and validating individualized HGI calculation tools to ultimately facilitate the transition of HGI from a research indicator to a practical clinical instrument.

Data Sharing Statement

Data availability is not applicable as no data was generated in this communication.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work. The specific contributions of each author are as follows:

Yue Ren: Conceptualization, Writing-Original Draft.

Zhiyi Chen: Data Curation, Visualization, Formal Analysis, Writing-Review & Editing.

Bin Wang: Supervision, Writing-Review & Editing, Project Administration.

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Disclosure

The authors declare no conflicts of interest in this communication.

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