COMMENT ON TANG ET AL.

The Impact of Carbamylation and Anemia on HbA_{1c}'s Association With Renal Outcomes in Patients With Diabetes and Chronic Kidney Disease. Diabetes Care 2023;46:130–137

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We were interested in the recent article in *Diabetes Care* from Tang et al. (1), in which they reported that lower HbA_{1c} in subjects with highly carbamylated albumin (C-Alb) was not clearly related to glucose levels, precluding a relationship of HbA_{1c} with the later progression of chronic kidney disease.

Their findings accord well with the in vitro description of glycation and carbamylation competing for the modification of proteins (2). Despite carbamylated hemoglobin not being directly measured, we can hypothesize that C-Alb reflected carbamylated hemoglobin in the participants of the Chronic Renal Insufficiency Cohort (CRIC), which reduced their HbA_{1c} and probably influenced the anemia of some subjects (3).

The carbamylation of protein and the anemia that develops with the progression of diabetic kidney disease (DKD) can therefore lead to HbA_{1c} measurements underestimating the true glucose exposure, contributing to its poor reliability as an indicator of glucose control in end-stage renal disease (4). The underestimation may also explain why glucose control fails to slow the decline of renal function despite its favorable effect on albuminuria (5).

As discussed by Tang et al. (1), there is no simple alternative to the measurement of HbA_{1c} in DKD. Other circulating proteins are also altered by carbamylation. However, we can expect that carbamylation occurs preferentially at late stages of DKD due to the retention of urea, and DKD stages 2, 3A, 3B, and 4 were represented in the CRIC cohort. The authors can probably help clinicians by providing a simple table, similar to Table 1 in their article, in which they replace the quartiles of HbA_{1c} by stages of DKD and report C-Alb, HbA_{1c}, and their relation to random glucose and later progression of DKD. Then we would know whether HbA_{1c} is biased by carbamylation only at stage 4 or sooner than that.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

References

1. Tang M, Berg A, Rhee EP, et al. The impact of carbamylation and anemia on HbA_{1c}'s association with renal outcomes in patients with diabetes and chronic kidney disease. Diabetes Care 2023; 46:130–137
2. Nicolas C, Jaisson S, Gorisse L, et al. Carbamylation is a competitor of glycation for protein modification in vivo. Diabetes Metab 2018;44: 160–167
3. Kalim S, Tamez H, Wenger J, et al. Carbamylation of serum albumin and erythropoietin resistance in end stage kidney disease. Clin J Am Soc Nephrol 2013;8:1927–1934
4. Riveline JP, Teynie J, Belmouaz S, et al. Glycaemic control in type 2 diabetic patients on chronic haemodialysis: use of a continuous glucose monitoring system. Nephrol Dial Transplant 2009; 24:2866–2871
5. Karalliedde J, Winocour P, Chowdhury TA, et al. Clinical practice guidelines for management of hyperglycaemia in adults with diabetic kidney disease. Diabet Med 2022; 39:e14769

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