

# Prognostic Value of Hemoglobin Concentration on Renal Outcomes with Diabetic Kidney Disease: A Retrospective Cohort Study [Letter]

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## Dear editor

Chen et al recently conducted an interesting study examining the relationship between hemoglobin concentrations and the risk of kidney function decline in patients with diabetic kidney disease (DKD).<sup>1</sup> Their findings revealed an inverse, albeit non-linear, association between hemoglobin levels and the risk of kidney failure. While these results offer valuable insights, we believe that a more comprehensive analysis could enhance the interpretability and robustness of their findings.

Based on Table 1 from Chen et al's study,<sup>1</sup> it was observed that patients with lower hemoglobin levels exhibited significantly poorer kidney function, as evidenced by elevated serum cystatin C ( $p < 0.001$ ) and creatinine ( $p < 0.001$ ) concentrations, as well as reduced proteinuria severity ( $p < 0.001$ ), compared to those with higher hemoglobin levels. Consequently, it would be anticipated that individuals with lower hemoglobin levels would face a heightened risk of composite kidney outcomes, as demonstrated by Chen et al. To ascertain the independent impact of hemoglobin concentration on kidney outcomes in renally impaired patients, it is crucial to control for potential confounders such as baseline kidney function disparities. Regrettably, in their multivariate analyses, Chen et al did not adjust for serum creatinine or estimated glomerular filtration rate (eGFR), leaving a significant gap in their findings. We recommend that the authors conduct additional statistical analyses (eg, a new model IV) to validate the robustness and validity of their results.

Furthermore, Chen et al reported a non-linear relationship between hemoglobin levels and kidney risk, pinpointing an inflection point. We posit that this intriguing observation may be attributed to variations in the etiology of anemia across different patient groups. The pathogenesis of anemia in patients with DKD is multifactorial, encompassing factors such as inadequate erythropoietin production, chronic inflammation with dysregulated iron metabolism, concomitant morbidities predisposing to anemia, hyperparathyroidism, and nutritional deficiencies affecting erythropoietic efficiency.<sup>2</sup> The etiology and severity of anemia are likely to evolve with declining kidney function; for instance, previous studies have indicated that dialysis-dependent patients exhibit a significantly higher incidence of peptic ulcer bleeding compared to those with chronic kidney disease (CKD).<sup>3</sup> Advanced CKD is also associated with an increased likelihood of functional iron deficiency but a decreased likelihood of absolute iron deficiency.<sup>4</sup> These observations imply that the underlying causes and contributors to anemia may vary according to the severity of kidney dysfunction. Therefore, the identified inflection point in Chen et al's study could potentially serve as a threshold demarcating different etiologies of anemia across varying degrees of kidney functions. We recommend that, if feasible, the authors can include additional hematological indices, such as mean corpuscular volume and iron profiles, to elucidate the origins of anemia and provide deeper insights into the biologic implications of the observed non-linear relationship.

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## Disclosure

The author reports no conflicts of interest in this communication.

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