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Letter to the Editor

From proteinuria to prediction: Reassessing biomarkers in type 2 diabetic nephropathy

Dear Editor,

We read with keen interest the article by Hliel et al., titled "Assessment and prediction of diabetic kidney disease (DKD) in patients with type 2 diabetes mellitus by using advanced biomarkers" (Nefrologia, 2025).[1] The authors focus on monocyte chemoattractant protein-1 (MCP-1) and WISP1 as predictive biomarkers for early-stage DKD is both timely and significant given the global burden of diabetic complications. This study contributes important data from the Middle Eastern population, a region underrepresented in biomarker-based nephrology research. While the findings offer valuable clinical insights, a few methodological and interpretive considerations merit discussion for further strengthening future research.

The authors employed a cross-sectional case control design involving 180 participants divided into normo-, micro-, and macroalbuminuric groups. However, the study's cross-sectional nature limits causal inference. A longitudinal cohort design would more robustly establish temporal relationships between biomarker levels and DKD progression, as demonstrated by Sabanayagam et al. in a machine-learning-based prospective analysis on DKD risk in Asian adults.[2] Additionally, the study included diabetic patients aged ≥40 years with disease durations ranging widely. However, age and duration of diabetes are significant independent variables for DKD onset. Adjusting for these covariates in multivariate models would provide clearer associations between biomarkers and renal function decline.

The study identifies MCP-1 as a highly sensitive and specific marker for all DKD stages, with an AUC approaching 1.0. However, such perfect diagnostic performance raises concern about overfitting or population-specific confounders. Independent external validation across geographically and ethnically diverse cohorts is critical before recommending clinical implementation, as per the recommendations of Devarajan et al. regarding biomarker translation in nephrology.[3] Furthermore, while WISP1 was proposed as a prognostic marker, its relatively low specificity in normoalbuminuric patients (51%) limits its utility in early screening. Additional studies are needed to delineate whether WISP1 elevation reflects systemic metabolic dysregulation or is kidney-specific.

The study notably omits kidney biopsy data. Although biopsy is not routinely performed in early DKD, even limited histological validation would offer a mechanistic basis for the observed biomarker elevations. This is especially relevant for WISP1, a member of the Wnt signalling cascade, which is known to affect multiple organ systems beyond the kidney, including adipose and bone tissues.[4]

The authors rightly propose MCP-1 as a non-invasive, early diagnostic marker. However, they do not comment on cost, accessibility, or turnaround time for MCP-1 and WISP1 ELISA assays in routine clinical settings. For these biomarkers to shift paradigms in DKD screening, comparative cost-effectiveness analyses versus traditional markers (e.g., ACR, cystatin C) should be conducted, as emphasized by Rupprecht et al. in their 2024 review on non-invasive CKD biomarkers.[5]

In conclusion, the study by Hliel et al. advances the conversation around early DKD detection using immune-inflammatory and signalling biomarkers. MCP-1, in particular, holds promise as a non-invasive indicator of early renal insult. However, further multicentric, prospective studies with histopathological correlation and economic evaluations are needed to validate these findings and facilitate clinical integration.

Thank you for the opportunity to engage with this impactful work.

CRediT authorship contribution statement

SD: writing – original draft, writing – review & editing. HS: supervision, writing – review & editing. PA: conceptualization, Writing – review & editing.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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