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LETTER

A Comment on 'Clinical Value of Urinary Wilms' Tumour-1 and Mu-Glutathione S-Transferase Gene Expression in Kidney Injury in Type 2 Diabetes Mellitus: Important Considerations for Clinical Application' [Letter]

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Dear editor

We read with great interest the article by Cai et al titled "Clinical Value of Urinary Wilms' Tumour-1 and Mu-Glutathione S-Transferase Gene Expression in Kidney Injury in Type 2 Diabetes Mellitus".[1] While we commend the authors for their innovative work in exploring novel biomarkers for diabetic nephropathy detection, we would like to highlight several important limitations and propose constructive suggestions for future research.

The study presents several methodological limitations that warrant attention. First, the absence of longitudinal follow-up makes it impossible to evaluate the prognostic value of WT-1 and Mu-GST in positive patients. We suggest implementing a prospective cohort study design with standardized follow-up protocols, including fixed time points for assessment and unified evaluation criteria. This would better capture the predictive value of these biomarkers for disease progression.

Second, the study did not adequately consider common comorbidities, particularly hypertension and cardiovascular diseases, which significantly influence both biomarker expression and kidney function. Hypertension is not merely a common comorbidity but an independent risk factor for kidney injury, as sustained high blood pressure damages glomerular structures and accelerates renal function decline.[2] Similarly, cardiovascular diseases can compromise renal perfusion and contribute to kidney injury through multiple pathways, including hemodynamic alterations and inflammatory responses.[3] These factors should be considered as crucial covariates in analysis, with subgroup analyses performed to evaluate both their direct impact on biomarker expression and potential interactions with kidney disease progression.

Third, the study analyzed all diabetic nephropathy patients as a single group without considering their different chronic kidney disease (CKD) stages. Given that kidney function deteriorates progressively through CKD stages 1–5, biomarker expression patterns may vary significantly at different stages of disease progression.[4] Each CKD stage represents distinct pathophysiological changes, and the sensitivity and specificity of WT-1 and Mu-GST might differ accordingly. We propose conducting additional analyses stratified by CKD stages to establish stage-specific reference ranges and diagnostic thresholds. This would enable clinicians to more accurately interpret test results and provide stage-appropriate treatment recommendations.

Fourth, the study did not evaluate the impact of medications, such as ACEI/ARB therapy, which is a crucial treatment for diabetic nephropathy.[5] ACEI/ARB can modulate the renin-angiotensin-aldosterone system and potentially alter the pathophysiological processes in diabetic nephropathy, thereby affecting the expression patterns of WT-1 and Mu-GST.[5] The interaction between these medications and biomarker expression is particularly relevant. We recommend establishing

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a comprehensive medication documentation system that records not only the type and dosage of medications but also treatment duration and compliance. This would enable clinicians to accurately assess biomarker results in the context of ongoing medical therapy and ensure the reliable application of these promising biomarkers in patient care.

We believe addressing these limitations would significantly enhance the clinical utility of these promising biomarkers, providing more reliable evidence for early diagnosis and prognosis assessment in diabetic nephropathy. We look forward to future studies that incorporate these suggestions and further validate the clinical application of these biomarkers.

Disclosure

The authors report no conflicts of interest in this communication.

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