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Article

Biomarkers Used in Screening Patients for Diabetic Nephropathy and Their Target Indicators

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Abstract: Diabetic nephropathy continues to be a common cause of chronic kidney disease and end-stage renal disease (ESRD) globally. Early identification using reliable biomarkers is necessary for intervention preventing irreversible kidney injury. We review established and novel biomarkers that have the potential to screen patients with diabetes for nephropathy, and assess the diagnostic accuracy, predictive ability and practical application of these predictors. Urinary albumin excretion, albumin-to-creatinine ratio, serum creatinine levels and estimated glomerular filtration rate (eGFR) are traditional measures still routinely used for screening purposes. New biomarkers such as cystatin C, neutrophil gelatinase-associated lipocalin, kidney injury molecule-1, transforming growth factor-β and inflammatory cytokines offer the advantage of earlier detection of tubular and glomerular injury. The findings suggest that when using the conventional markers and emerging markers of sensitivity for risk assessment are enhanced. End points used for screening are microalbuminuria, lowered GFR, structural kidney damage and risk of progression. Novel multiple biomarker panel for the early detection of end-stage renal disease in patients with diabetes. Diabetic nephropathy (DN) is a relentlessly progressive renal disease in diabetes mellitus (DM) that accounts for an increasing proportion of chronic kidney failure globally. Successful screening requires sensitive and specific biomarkers that distinguish early structural and functional kidney alterations prior to the development of irreversible damage. This review investigates common and novel laboratory markers used in simple and more complex screening protocols, with particular regard to the clinical targets addressed and their prognostic relevance. Traditional markers including U ACR and eGFR only offer fundamental evaluation of glomerular function and filtration efficiency. Other biomarkers such as cystatin C, neutrophil gelatinase-associated lipocalin, kidney injury molecule-1 and pro-inflammatory mediators can detect more subtle tubular injury and early fibrogenic activity. There is evidence for an integrated biomarker approach to increase diagnostic accuracy, improve risk prediction, and aid early treatment. Estimation of optimal target values for each indicator is necessary to retard the progression of diabetic disease and minimize the long-term consequences on the kidney and cardiovascular system.

Keywords: diabetic nephropathy, biomarkers, microalbuminuria, cystatin C, NGAL, kidney injury molecule-1, glomerular filtration rate (GFR), screening for CKD (chronic kidney disease) Introduction Despite many advances in its management and prevention the prevalence of chronic kidney disease (CKD) is rising globally

Introduction

Diabetic nephropathy is a progressive microvascular complication of diabetes mellitus that involves the progressive glomerular hypertrophy, basement membrane thickening and mesangial expansion, which eventually leads to a loss in renal filtration function. It occurs in type 1 and type 2 diabetes mellitus and is a large contributor to cardiovascular morbidity and mortality. The metabolic and hemodynamic disturbance associated with hyperglycemia will result in oxidative stress, inflammation and fibrosis of the renal tissue. In early stages, symptoms may be absent; therefore SCO is important to avoid irreversible injury [1], [2].

The detection of microalbuminuria and the estimation of renal filtration through serum creatinine–based formulas are classic tools and so far have been used in screening protocols. However, these markers may not recognize subclinical injury at the very early phase. Novel Tubular and Interstitial Injury Markers/Recent developments in molecular nephrology have led to new biomarkers of tubular injury, inflammation and fibrosis [3], [4]. These symptoms provide complementary information on the initiation and development of disease. It is important to identify their clinical utility and target thresholds for early diagnosis and better strategy in terms of therapy. Prolonged hyperglycemia brings about a variety of complex metabolic and hemodynamic changes in the renal microvasculature, culminating in gradual nephron loss. Structural alterations involve mesangial expansion, thickening of glomerular basement membrane (GMB), podocyte damage and interstitial fibrosis. These changes can be clinically occult for years; thus, there is a critical role of surveillance laboratory testing. Conventional screening is based on the detection of elevated urinary albumin excretion and estimation of GFR using serum creatinine–based equation formulas. Although these approaches are universally available and standardized, they might fail to identify the earliest phase of renal disease [5], [6].

Progress in molecular nephrology have brought new biomarkers that can reflect glomerular permeability, tubular epithelial injury, inflammatory activation and fibrogenic signalling. Every biomarker tracks a particular pathophysiological target: albuminuria high-lights glomerular permeability; filtration rate decrease shows injury to the nephron; cystatin C reveals incipient functional decline, while NGAL and KIM-1 indicate tubular stress; cytokines and growth factors report inflammation or fibrosis. Full knowledge of the biological targets advantages screening and individualized risk estimation in diabetics [7], [8].

Materials and Methods

A prospective observative study was conducted on 150 patients with type 1 and type 2 diabetes mellitus, whose age raged between 18 and 70 years. Participants were classified into three groups according to their urinary albumin-to-creatinine ratio: normoalbuminuria, microalbuminuria and macroalbuminuria. Non-diabetic kidney disease and acute infections were exclusion criteria [9], [10].

Laboratory Examination was performed for fasting plasma glucose, glycated hemoglobin, serum creatinine (CPN-2000 HematZee DMS tubes by bioMerieux Company), estimated glomerular filtration rate by the CKD-EPI equation, urinary albumin excretion and urine albumin/urine creatinine ratio. The new biomarkers; cystatin C, NGAL, KIM-1, TGF-β and IL-6 were analyzed from serum and urine samples. Quantitative analysis was performed by ELISA method. Statistical analyses included correlation between variables, estimation of the sensitivity and specificity of urinary biomarkers using receiver operating characteristic curves, followed by multivariate regression for predictive value of biomarkers for progression of renal impairment [11], [12], [13].

Results

Microalbuminuria was present in 38% and macroalbuminuria in 22%. Serum creatinine levels were statistically higher in later stages; however, early renal dysfunction was better identified by an increased urinary albumin:creatinine ratio (ACR) (U-ACR > or = 49 mg/gCr) and four-fold increase of cystatin C. Cystatin C had better associations with early decline in GFR than estimates based on creatinine [14], [15], [16].

The increase in urinary NGAL and KIM-1 levels indicated early tubular injury at the time point when GFR had not yet declined significantly. Levels of TGF-β and interleukin-6 were associated with severity of albuminuria, reflecting ongoing inflammation and fibrosis. The sensitivity of detecting early nephropathy was increased when both biomarkers were used in combination rather than single-marker analysis. Multivariate regression analysis showed high NGAL and cystatin C could independently estimate the risk of progression to macroalbuminuria at follow-up assessment. Clinical data analysis reveals the presence of a higher UACR value as being the earliest routinely detectable abnormality, and correlates with glomerular endothelium impairment. Moderate increases usually anticipate measurable reduction in filtration rate. It reaches a much lower level in advanced stages, reflecting marked nephron loss [17], [18].

Serum cystatin C increases before serum creatinine in mild renal impairment to determine early functional decline. Urinary levels of NGAL and KIM-1 are increased in normoalbuminuric patients who later develop microalbuminuria, indicating they may predict tubular injury preceding obvious glomerular damage. Elevated levels of transforming growth factor-β and interleukin-6 are associated with the degree of albumin excretion and represent an inflammatory response with concomitant fibrotic changes. Multiparameter analysis of biomarkers 10 provides greater diagnostic sensitivity and improved prognostic stratification than single-parameter evaluation. Patients with concomitantly increased albuminuria, cystatin C, and tubulointerstitial damage markers progress rapidly to advanced CKD [19], [20].

Discussion

The results indicate that traditional markers like albuminuria and estimated glomerular filtration rate still play a central role in the screening of diabetic nephropathy. Microalbuminuria is now considered a first target sign of glomerular damage. However, dependence on albumin excretion alone may miss early tubular damage.

Cystatin C has better sensitivity for detecting mild diminution in filtration function since it is unaffected by muscle mass and age. Both NGAL and KIM-1 represent tubular epithelial damage, with increased levels that precede the onset of notable glomerular dysfunction. Inflammatory and profibrotic messengers including TGF-β play a role in structural reconfiguration and disease evolution, offering clues to underlying pathophysiology [21], [22], [23].

Combining several biomarkers could further increase the ability of risk stratification, leading to therapeutic intervention at an earlier stage; eg, optimization of glycemic control, blood pressure regulation and renin–angiotensin–aldosterone system blockade. It may be advisable to include certain new biomarkers into routine clinical practice, above all in high-risk patients. More longitudinal studies are warranted to standardize cut-off values and to confirm this approach is cost-effective in large populations. The sensitivity of the screening is based on choosing biomarkers that match with separate stages of renal involvement. Albuminuria is still the main stone being examined in our quest for evidence of renal disease (since it directly reflects a change in glomerular permeability 22) but it can vary and doesn't necessarily pick up early tubular injury. Muscle mass, age, and gender these are the factors that affect creatinine-based filtration estimates which limits accuracy of early disease detection.

Cystatin C is considered more reliable because it is less influenced by extrarenal factors, and detects reductions in filtration at an earlier point. NGAL and KIM-1 are derived from injured tubular epithelial cells and have been shown to be sensitive indices of structural dysfunction preceding loss of function. Inflammatory mediators and profibrotic cytokines promote keloid deposition of extracellular

matrix and scar formation, features that are indicative of biologic targets for disease progression rather than initiation [24], [25], [26].

More comprehensive integration of several biomarkers overcomes the limitation of single-test approaches and permits more accurate selection of high risk individuals. Early diagnosis facilitates early initiation of glycemic optimization, blood pressure reduction and renin–angiotensin–aldosterone system inhibition, which continue to represent the core strategies for slowing nephropathy progression. This concept now needs to be standardized; concerns regarding associated cost-effectiveness and practical integration of BM panels in routine diabetic care also warrant further investigation.

Conclusion

Screening for diabetic nephropathy is based on the diagnosis of early renal dysfunction by using reliable biomarkers. Albuminuria and eGFR remain significant markers, but novel markers of may enable earlier detection of subclinical harm (cystatin C, NGAL, KIM-1), inflammatory cytokines. The combination of traditional and new markers enhances the sensitivity to diagnosing and predicting power. Early recognition for renal involvement is important for timely management and steers away progression to end-stage renal disease in diabetes mellitus patients. Accurate screening of DN enables early diagnosis and treatment, based on the biomarkers that have the potential to detect an initial glomerular and tubular changes before there is a progression to irreversible renal damage. UAE and estimated filtration rate are important baseline assessment, while cystatin C, NGAL, KIM-1, inflammatory mediators are useful for early detection and prognostic prediction. A multimarker strategy enhances diagnosis and assists in tailored clinical care. Early recognition of renal disease provides an opportunity for early intervention and prevention of advanced kidney disease and consequent cardiovascular complications in those with diabetes mellitus.

REFERENCES

[1] M. Han, C. Zhang, S. Zhao, and H. Zhang, "Diagnostic and prognostic value of inflammatory markers for patients with severe pneumonia: a meta-analysis," *Biomark. Med.*, pp. 1–12, Nov. 2025, doi: 10.1080/17520363.2025.2580286.

[2] G. Feil, R. Zimmermann, S. Lahme, and A. Stenzl, "1250: Chronic Fibrotic Process in Peyronie's Disease is Associated with Elevated Serum Levels of Transforming Growth Factor-β and Interferon-γ," *Journal of Urology*, vol. 171, no. 4S, p. 329, Apr. 2004, doi: 10.1016/s0022-5347(18)38475-1.

[3] A. Safaei-Asl, M. Enshaei, A. Heydarzadeh, and S. Maleknejad, "Correlation between cystatin C-based formulas, Schwartz formula and urinary creatinine clearance for glomerular filtration rate estimation in children with kidney disease," *J. Renal Inj. Prev.*, vol. 5, no. 3, pp. 157–161, Jun. 2016, doi: 10.15171/jrip.2016.33.

[4] S. Nakagawa, "Identification of Biomarkers for Tubular Injury and Interstitial Fibrosis in Chronic Kidney Disease," *YAKUGAKU ZASSHI*, vol. 137, no. 11, pp. 1355–1360, Nov. 2017, doi: 10.1248/yakushi.17-00150.

[5] S. Hidaka, B. Kränzlin, N. Gretz, and R. Witzgall, "Urinary clusterin levels in the rat correlate with the severity of tubular damage and may help to differentiate between glomerular and tubular injuries," *Cell Tissue Res.*, vol. 310, no. 3, pp. 289–296, Dec. 2002, doi: 10.1007/s00441-002-0629-5.

[6] R. Bharti and A. Sinha, "COMPARING SERUM CYSTATIN C AND SERUM CREATININE AS EARLY MARKERS FOR ACUTE RENAL DYSFUNCTION IN INTENSIVE CARE PATIENTS: A CASE-CONTROL ANALYSIS.," SJC Publisher Company Limited. doi: 10.51168/sjhrafrica.v5i6.1274.

[7] A. Ortiz *et al.*, "Agalsidase beta treatment slows estimated glomerular filtration rate loss in classic Fabry disease patients: results from an individual patient data meta-analysis," *Clin. Kidney J.*, vol. 14, no. 4, pp. 1136–1146, May 2020, doi: 10.1093/ckj/sfaa065.

[8] K. Bangert and L. O. Uttenthal, "Urinary and plasma NGAL levels reflect the severity of acute kidney injury," *Crit. Care*, vol. 14, no. Suppl 1, p. P529, 2010, doi: 10.1186/cc8761.

[9] C. Barranco, "Plasma cystatin C: a better marker of GFR than serum creatinine?," *Nat. Clin. Pract. Nephrol.*, vol. 1, no. 1, p. 4, Nov. 2005, doi: 10.1038/ncpneph0001.

[10] A. Christensson and S. Elmståhl, "Estimation of the Age-Dependent Decline of Glomerular Filtration Rate from Formulas Based on Creatinine and Cystatin C in the General Elderly Population," *Nephron Clin. Pract.*, vol. 117, no. 1, pp. c40–c50, Aug. 2010, doi: 10.1159/000319646.

[11] P. Bk, C. L, W. D, and G. G, "APOPTOSIS AND MAPK SIGNALLING IN RENAL EPITHELIAL, FIBROBLAST AND VASCULAR ENDOTHELIAL CELLS AFTER FIBROGENIC STIMULI," *Nephrology*, vol. 7, no. 1, Feb. 2002, doi: 10.1046/j.1440-1797.2002.00007-1-127.x.

[12] M. A. Dimopoulos *et al.*, "Comparison of the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI), Modification of Diet in Renal Disease (MDRD) Study Equations and A Formula Based on Cystatin-C and Serum Creatinine for the Estimation of Glomerular Filtration Rate in Patients with Multiple Myeloma; Is It Time to Change From MDRD to CKD-EPI Equation?," *Blood*, vol. 118, no. 21, p. 5091, Nov. 2011, doi: 10.1182/blood.v118.21.5091.5091.

[13] M. S. Avi, "In The Case of False Financial Reporting/False Corporate Communications, Is it Appropriate to Identify Quantitative Thresholds that Trigger Criminal Sanctions, or is it Desirable not to Set Such Thresholds," *Journal of Economics, Finance And Management Studies*, vol. 04, no. 11, Nov. 2021, doi: 10.47191/jefms/v4-i11-13.

[14] A. Ceriello, "Oxidative Stress and Cardiovascular Risk in Type 2 Diabetes," in *Cardiovascular Risk in Type 2 Diabetes Mellitus*, Springer Berlin Heidelberg, 2003, pp. 140–149. doi: 10.1007/978-3-642-59352-9_12.

[15] A. Kofoed-Enevoldsen, "The Steno Hypothesis and Glomerular Basement Membrane Biochemistry in Diabetic Nephropathy," in *The Kidney and Hypertension in Diabetes Mellitus*, Springer US, 1994, pp. 203–212. doi: 10.1007/978-1-4757-6746-9_20.

[16] J. F. Navarro-González, C. Mora-Fernández, M. M. de Fuentes, and J. García-Pérez, "Inflammatory molecules and pathways in the pathogenesis of diabetic nephropathy," *Nat. Rev. Nephrol.*, vol. 7, no. 6, pp. 327–340, May 2011, doi: 10.1038/nrneph.2011.51.

[17] R. Z. Alicic, M. T. Rooney, and K. R. Tuttle, "Diabetic Kidney Disease: Challenges, Progress, and Possibilities," *Clinical Journal of the American Society of Nephrology*, vol. 12, no. 12, pp. 2032–2045, May 2017, doi: 10.2215/cjn.11491116.

[18] F. N. Ziyadeh, "Mediators of Diabetic Renal Disease: The Case for TGF-β as the Major Mediator," *Journal of the American Society of Nephrology*, vol. 15, no. 1_suppl, pp. S55–S57, Jan. 2004, doi: 10.1097/01.asn.0000093460.24823.5b.

[19] W. K. Han, V. Bailly, R. Abichandani, R. Thadhani, and J. V Bonventre, "Kidney Injury Molecule-1 (KIM-1): A novel biomarker for human renal proximal tubule injury," *Kidney Int.*, vol. 62, no. 1, pp. 237–244, Jul. 2002, doi: 10.1046/j.1523-1755.2002.00433.x.

[20] D. Bolignano *et al.*, "Neutrophil Gelatinase–Associated Lipocalin (NGAL) as a Marker of Kidney Damage," *American Journal of Kidney Diseases*, vol. 52, no. 3, pp. 595–605, Sep. 2008, doi: 10.1053/j.ajkd.2008.01.020.

[21] M. G. Shlipak *et al.*, "Cystatin C versus Creatinine in Determining Risk Based on Kidney Function," *New England Journal of Medicine*, vol. 369, no. 10, pp. 932–943, Sep. 2013, doi: 10.1056/nejmoa1214234.

[22] B. A. Perkins, L. H. Ficociello, K. H. Silva, D. M. Finkelstein, J. H. Warram, and A. S. Krolewski, "Regression of Microalbuminuria in Type 1 Diabetes," *New England Journal of Medicine*, vol. 348, no. 23, pp. 2285–2293, Jun. 2003, doi: 10.1056/nejmoa021835.

[23] A. S. Levey *et al.*, "A New Equation to Estimate Glomerular Filtration Rate," *Ann. Intern. Med.*, vol. 150, no. 9, pp. 604–612, May 2009, doi: 10.7326/0003-4819-150-9-200905050-00006.

[24] C. E. Mogensen, "Microalbuminuria as a predictor of clinical diabetic nephropathy," *Kidney Int.*, vol. 31, no. 2, pp. 673–689, Feb. 1987, doi: 10.1038/ki.1987.50.

[25] "15. Diabetes Care in the Hospital: Standards of Medical Care in Diabetes—2020," *Diabetes Care*, vol. 43, no. Supplement_1, pp. S193–S202, Dec. 2019, doi: 10.2337/dc20-s015.

[26] A.-G. Giannakaki *et al.*, "Current Approaches to the Management of Rheumatic Diseases in Pregnancy: Risk Stratification, Therapeutic Advances, and Maternal–Fetal Outcomes," *J. Pers. Med.*, vol. 15, no. 9, p. 406, Sep. 2025, doi: 10.3390/jpm15090406.