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DIABETIC NEPHROPATHY: EARLY LABORATORY DIAGNOSIS AND PROGNOSTIC POTENTIAL OF BIOMARKERS (A REVIEW)

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Introduction

Diabetes mellitus (DM) remains one of the most pressing global public health challenges due to its rapidly increasing prevalence and the high burden of chronic complications. Among these complications, diabetic nephropathy (DN) is one of the most severe and common microvascular disorders, affecting approximately 30–40% of patients with both type 1 and type 2 diabetes. DN is a leading cause of end-stage renal disease (ESRD) worldwide and significantly contributes to cardiovascular morbidity and mortality.

Early identification of diabetic nephropathy, particularly at the preclinical stage, is crucial for preventing irreversible renal damage and improving long-term outcomes. Traditionally, microalbuminuria has been considered the earliest clinical marker of DN. However, accumulating evidence suggests that structural and functional renal changes may precede the onset of albuminuria. Consequently, there is growing interest in novel biomarkers that reflect glomerular and tubular injury, inflammation, and oxidative stress, enabling earlier diagnosis and more accurate prediction of disease progression.

This review aims to analyze current evidence regarding early laboratory biomarkers of diabetic nephropathy and to evaluate their diagnostic and prognostic significance.

Pathogenesis of Diabetic Nephropathy and the Role of Microalbuminuria

The development of diabetic nephropathy is driven by a complex interplay of metabolic, hemodynamic, and inflammatory mechanisms. Chronic hyperglycemia plays a central role by inducing advanced glycation end products, oxidative stress, and activation of pro-inflammatory signaling pathways. These processes ultimately result in glomerular hypertrophy, thickening of the glomerular basement membrane, mesangial expansion, and progressive renal fibrosis.

Microalbuminuria has long been regarded as a hallmark of early diabetic nephropathy and a predictor of renal and cardiovascular risk. In patients with type 1 diabetes, microalbuminuria often reflects early glomerular damage. However, in type 2 diabetes, albuminuria may also be influenced by systemic endothelial dysfunction and comorbid cardiovascular disease, limiting its specificity for renal injury.

Furthermore, a substantial proportion of diabetic patients exhibit declining glomerular filtration rate (GFR) in the absence of albuminuria, a condition referred to as non-albuminuric diabetic nephropathy. These observations highlight the need for more sensitive biomarkers capable of detecting renal injury before overt albuminuria develops.

Biomarkers of Tubular Injury

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Recent studies have emphasized the importance of tubular damage in the early stages of diabetic nephropathy. Tubular injury biomarkers may appear earlier than glomerular markers and provide valuable prognostic information.

Cystatin C is a low-molecular-weight protein freely filtered by the glomeruli and almost completely reabsorbed by proximal tubules. Serum cystatin C is considered a more sensitive indicator of GFR decline than serum creatinine, as it is less influenced by age, sex, and muscle mass. Elevated urinary cystatin C reflects impaired tubular reabsorption and early tubular dysfunction.

N-acetyl-β-D-glucosaminidase (NAG) is a lysosomal enzyme released from damaged proximal tubular epithelial cells. Increased urinary NAG levels have been reported in diabetic patients with normoalbuminuria, suggesting its utility as an early marker of tubular injury and a predictor of nephropathy progression.

Neutrophil gelatinase-associated lipocalin (NGAL) is rapidly upregulated in response to renal injury. Both serum and urinary NGAL concentrations have been shown to increase in the early stages of diabetic nephropathy, even before the onset of microalbuminuria, indicating subclinical renal damage.

Other promising tubular biomarkers include kidney injury molecule-1 (KIM-1) and α1-microglobulin, which are associated with tubular inflammation and fibrosis and correlate with disease severity.

Glomerular Biomarkers and Extracellular Matrix Components

Persistent hyperglycemia leads to dysregulation of extracellular matrix turnover and excessive accumulation of fibrotic components within the glomeruli. As a result, several glomerular biomarkers have been proposed for the early detection of diabetic nephropathy.

Urinary excretion of type IV collagen has been identified as a sensitive marker of glomerular basement membrane remodeling and early renal fibrosis. Multiple studies have demonstrated that urinary collagen IV levels increase prior to the development of microalbuminuria and are closely associated with the progression of nephropathy.

Additional glomerular biomarkers, such as laminin, transferrin, immunoglobulin G (IgG), and ceruloplasmin, reflect increased glomerular permeability and structural damage. Their combined assessment may improve diagnostic accuracy, particularly in patients with atypical disease progression.

Inflammatory and Oxidative Stress Biomarkers

Growing evidence supports the role of chronic low-grade inflammation in the pathogenesis of diabetic nephropathy. Elevated levels of pro-inflammatory cytokines, including interleukin-6 (IL-6), interleukin-8 (IL-8), tumor necrosis factor-alpha (TNF-α), and monocyte chemoattractant protein-1 (MCP-1), have been detected in both serum and urine of patients with diabetic

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nephropathy. These mediators contribute to renal inflammation, endothelial dysfunction, and fibrotic remodeling.

Oxidative stress is another key mechanism underlying diabetic renal injury. Biomarkers such as 8-hydroxy-2′-deoxyguanosine (8-OHdG) reflect oxidative DNA damage and have been associated with disease severity and progression. The integration of inflammatory and oxidative stress markers into diagnostic algorithms may enhance risk stratification and prognostic assessment.

Conclusion

The evidence reviewed in this article indicates that while microalbuminuria remains a valuable clinical marker, it is insufficient as a standalone tool for the early detection of diabetic nephropathy. Novel biomarkers reflecting tubular injury, glomerular remodeling, inflammation, and oxidative stress provide deeper insight into the underlying pathophysiology and enable earlier diagnosis.

A multimarker approach incorporating cystatin C, NGAL, NAG, KIM-1, type IV collagen, and inflammatory mediators holds significant promise for improving the prediction of disease progression and guiding individualized therapeutic strategies. The implementation of such biomarker panels in routine clinical practice may contribute to more effective prevention of end-stage renal disease in patients with diabetes.

References:

1. Junqueira, L. C., & Carneiro, J. (2022). Basic Histology: Text & Atlas (16th ed.). McGraw-Hill Education.
2. Kumar, V., Abbas, A. K., & Aster, J. C. (2022). Robbins and Cotran Pathologic Basis of Disease (10th ed.). Elsevier.
3. Fioretto, P., & Mauer, M. (2007). Histopathology of diabetic nephropathy. Seminars in Nephrology, 27(2), 195–207.
4. Ergasheva, G. (2025). POLYCYSTIC OVARY SYNDROME: A COMPREHENSIVE OVERVIEW AND CURRENT TREATMENT APPROACHES. Modern Science and Research, 4(4), 937-944.
5. Ergasheva, G. (2025). ACROMEGALY: A SEVERE NEUROENDOCRINE DISORDER WITH MULTISYSTEM MANIFESTATIONS. Modern Science and Research, 4(3), 1123-1131.
6. Ergasheva, G. (2024). THE ROLE OF CORRECTIONAL PEDAGOGY IN ORGANIZING THE EDUCATION OF CHILDREN WITH DISABILITIES. Ethiopian International Journal of Multidisciplinary Research, 11(06), 206-207.
7. Toxirovna, E. G. (2024). QALQONSIMON BEZ KASALLIKLARIDAN HASHIMOTO TIREODIT KASALLIGINING MORFOFUNKSIONAL O'ZIGA XOSLIGI. Modern education and development, 16(7), 120-135.
8. Toxirovna, E. G. (2024). REVMATOID ARTRIT: BO'G'IMLAR YALLIG'LANISHINING SABABLARI, KLINIK BELGILARI, OQIBATLARI VA ZAMONAVIY DAVOLASH YONDASHUVLARI. Modern education and development, 16(7), 136-148.

AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES
ISSN NUMBER: 2692 - 5206 Volume 5. No 12. December ,2025

9. Эргашева, Г. Т. (2024). ОЦЕНКА КЛИНИЧЕСКОЙ ЭФФЕКТИВНОСТИ ОРЛИСТАТА У БОЛЬНЫХ ОЖИРЕНИЕМ И АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИЕЙ. Modern education and development, 16(7), 92-105.
10. Ergasheva, G. T. (2024). THE SPECIFICITY OFAUTOIMMUNE THYROIDITIS IN PREGNANCY. European Journal of Modern Medicine and Practice, 4(11), 448-453.
11. Эргашева, Г. Т. (2024). ИССЛЕДОВАНИЕ ФУНКЦИИ ЩИТОВИДНОЙ ЖЕЛЕЗЫ ПРИ ТИРЕОИДИТЕ ХАШИМОТО. Modern education and development, 16(7), 106-119.
12. Toxirovna, E. G. (2024). GIPOFIZ ADENOMASINI NAZORAT QILISHDA KONSERVATIV JARROHLIK VA RADIATSIYA TERAPIYASINING UZOQ MUDDATLI SAMARADORLIGI. Modern education and development, 16(7), 79-91.
13. ERGASHEVA, G. T. (2024). OBESITY AND OVARIAN INSUFFICIENCY. Valeology: International Journal of Medical Anthropology and Bioethics, 2(09), 106-111.
14. Ergasheva, G. T. (2024). Modern Methods in the Diagnosis of Autoimmune Thyroiditis. American Journal of Bioscience and Clinical Integrity, 1(10), 43-50.
15. Tokhirovna, E. G. (2024). COEXISTENCE OF CARDIOVASCULAR DISEASES IN PATIENTS WITH TYPE 2 DIABETES. TADQIQOTLAR. UZ, 40(3), 55-62.
16. Toxirovna, E. G. (2024). DETERMINATION AND STUDY OF GLYCEMIA IN PATIENTS WITH TYPE 2 DIABETES MELLITUS WITH COMORBID DISEASES. TADQIQOTLAR. UZ, 40(3), 71-77.
17. Toxirovna, E. G. (2024). XOMILADORLIKDA QANDLI DIABET KELTIRIB CHIQARUVCHI XAVF OMILLARINI ERTA ANIQLASH USULLARI. TADQIQOTLAR. UZ, 40(3), 63-70.
18. Toxirovna, E. G. (2024). QANDLI DIABET 2-TIP VA KOMORBID KASALLIKLARI BO'LGAN BEMORLARDA GLIKEMIK NAZORAT. TADQIQOTLAR. UZ, 40(3), 48-54.
19. Tokhirovna, E. G. (2024). MECHANISM OF ACTION OF METFORMIN (BIGUANIDE) IN TYPE 2 DIABETES. JOURNAL OF HEALTHCARE AND LIFE-SCIENCE RESEARCH, 3(5), 210-216.
20. Tokhirovna, E. G. (2024). THE ROLE OF METFORMIN (GLIFORMIN) IN THE TREATMENT OF PATIENTS WITH TYPE 2 DIABETES MELLITUS. EUROPEAN JOURNAL OF MODERN MEDICINE AND PRACTICE, 4(4), 171-177.