DIABETIC NEPHROPATHY: PATHOPHYSIOLOGICAL MECHANISMS AND MODERN APPROACHES TO MANAGEMENT

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Abstract. Diabetic nephropathy (DN) is one of the most serious chronic complications of diabetes mellitus and a leading cause of end-stage renal disease (ESRD) worldwide. The progression of DN is driven by metabolic, hemodynamic, and inflammatory mechanisms that affect glomerular and tubular structures. The purpose of this review is to summarize the modern understanding of DN pathophysiology, highlight diagnostic challenges, and discuss therapeutic approaches, including findings from recent regional studies emphasizing the interrelationship between diabetic nephropathy and anemia.

Keywords: diabetic nephropathy, diabetes mellitus, renal damage, anemia, oxidative stress, erythropoietin, chronic kidney disease

Introduction. Diabetic nephropathy (DN) remains one of the most common microvascular complications of diabetes mellitus and a significant cause of morbidity and mortality among patients with type 1 and type 2 diabetes. Epidemiological studies show that approximately 30–40% of patients with diabetes develop some degree of kidney involvement during the disease course [1]. The condition represents a continuum from microalbuminuria to overt proteinuria, progressive renal insufficiency, and eventually ESRD requiring dialysis or transplantation. Recent research highlights the importance of early

detection and comprehensive management of DN, which includes not only strict glycemic control but also correction of associated anemia and cardiovascular risk factors [2–4].

Epidemiology and risk factors. The global prevalence of DN varies according to population, genetics, and lifestyle factors. DN accounts for nearly 40% of all new cases of ESRD in developed countries [1]. The major risk factors include chronic hyperglycemia, hypertension, dyslipidemia, obesity, and genetic predisposition. It has been shown that the duration of diabetes and poor glycemic control are directly correlated with the development of nephropathy. Smoking, high salt intake, and insulin resistance further contribute to disease progression. In recent years, attention has been drawn to the role of anemia as a comorbid factor in DN. Studies conducted in Central Asia revealed a high frequency of anemia in diabetic patients with early signs of nephropathy, indicating that erythropoietin deficiency may begin even before overt renal failure [3,4].

Pathogenesis. The pathophysiology of diabetic nephropathy is multifactorial. Chronic hyperglycemia triggers a cascade of metabolic disturbances that lead to glomerular and tubular damage. The main mechanisms include:

Hyperglycemia-induced oxidative stress, resulting in excessive production of reactive oxygen species (ROS) that damage endothelial and mesangial cells.

Formation of advanced glycation end-products (AGEs), which alter extracellular matrix proteins, increase basement membrane thickness, and promote inflammation [5]. Activation of the renin–angiotensin–aldosterone system (RAAS), causing glomerular hypertension and fibrosis. Inflammatory cytokine release, such as interleukin-6 and tumor necrosis factor-α, which exacerbate tissue injury. In addition to these mechanisms, nephropathy is frequently accompanied by anemia, primarily due to decreased erythropoietin production

by damaged kidneys [3,4]. The resulting tissue hypoxia further accelerates fibrosis and nephron loss.

Clinical manifestations and diagnosis. Diabetic nephropathy progresses through several stages: hyperfiltration, microalbuminuria, overt proteinuria, and decline of glomerular filtration rate (GFR). Early stages are asymptomatic, which makes routine screening essential. The diagnosis of DN is primarily based on the detection of persistent albuminuria (≥30 mg/day) and reduced eGFR (<60 mL/min/1.73 m²). However, these indicators may not reflect early renal involvement. Therefore, novel biomarkers such as cystatin C, β2-microglobulin, and neutrophil gelatinase-associated lipocalin (NGAL) have been proposed to improve diagnostic accuracy [6].

Regional studies suggest that evaluating hemoglobin and erythropoietin levels alongside kidney function parameters provides valuable information for early diagnosis [2–4].

Management and therapeutic approaches. The management of diabetic nephropathy requires a comprehensive strategy addressing hyperglycemia, hypertension, dyslipidemia, and anemia.

1. Glycemic control.

Tight control of blood glucose remains the cornerstone of DN prevention. Both insulin therapy and oral hypoglycemic agents (such as metformin and DPP-4 inhibitors) reduce microvascular complications when target HbA1c levels (<7%) are maintained.

2. Blood pressure management.

RAAS blockade with ACE inhibitors or angiotensin receptor blockers (ARBs) reduces intraglomerular pressure and proteinuria, slowing disease progression

[7]. The recommended blood pressure goal is <130/80 mmHg for most diabetic patients.

3. Lipid regulation.

Statin therapy helps decrease oxidative stress and inflammation, offering additional renal protection.

4. Correction of anemia.

Erythropoiesis-stimulating agents (ESAs) and iron supplementation are essential components of therapy for diabetic patients with anemia. Several studies emphasize that early correction of anemia prevents further decline in renal function and improves quality of life [3,8].

5. New pharmacological agents.

Recent clinical trials demonstrate that sodium-glucose cotransporter 2 (SGLT2) inhibitors and glucagon-like peptide-1 receptor agonists (GLP-1 RAs) exert renoprotective effects beyond glycemic control [7]. They reduce intraglomerular pressure, inflammation, and fibrosis, thereby delaying ESRD.

Discussion. The interplay between diabetic nephropathy and anemia represents an important yet underrecognized aspect of diabetes management. Regional studies have contributed significantly to understanding this association, suggesting that monitoring hematological indices alongside renal parameters should become standard practice in diabetic care [2–4,8]. Anemia correction not only improves oxygen delivery but also reduces the activation of hypoxia-inducible factors and oxidative stress within renal tissue. Consequently, patients with timely correction of anemia demonstrate slower progression to ESRD compared to those without such intervention [9].

Conclusion. Diabetic nephropathy remains a major clinical and public health problem. Despite substantial progress in understanding its mechanisms, early

detection and integrated management remain challenges. Evidence indicates that combining conventional nephroprotective strategies with anemia correction and novel pharmacotherapies can significantly improve renal outcomes.

Future research should focus on identifying genetic and molecular markers of susceptibility, optimizing individualized treatment plans, and expanding preventive programs for at-risk diabetic populations.

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