Special journal of the Medical Academy and other Life Sciences
Vol. 3 No. 5 (2025)

Modern approaches to the management of patients with diabetic nephropathy.

Vaibhav Gumber[1], Ghassan Salibi[2], Nikolaos Tzenios[3]

[1] Kursk State Medical. University

[123] Charisma University

Abstract

Background: Diabetic nephropathy (DN), a major complication of diabetes mellitus, is one of the leading causes of chronic kidney disease (CKD) and end-stage renal disease (ESRD) worldwide. The increasing global burden of diabetes, especially in low- and middle-income countries, has led to a parallel rise in diabetic kidney disease. This study reviews current evidence-based strategies for the diagnosis, prevention, and management of DN, highlighting recent advances in pharmacological therapies, biomarker discovery, and the integration of precision medicine.

Methods and Materials: This project employed a comprehensive literature review using reputable databases including PubMed, Cochrane Library, Scopus, and guidelines from KDIGO and the American Diabetes Association. The methodology also involved synthesis of clinical trial data, expert consensus documents, and emerging research on novel therapeutic targets and biomarkers. Practical recommendations were developed through analysis and comparative evaluation of diagnostic and treatment algorithms.

Results: Findings indicate that DN pathogenesis is multifactorial, involving hyperglycemia, oxidative stress, and dysregulated hemodynamics. Key diagnostic tools such as urine albumin-to-creatinine ratio (UACR), estimated glomerular filtration rate (eGFR), and emerging biomarkers (e.g., NGAL, KIM-1, and urinary nephrin) enhance early detection. Novel pharmacotherapies demonstrate renoprotective and cardioprotectiveincluding SGLT2 inhibitors, GLP-1 receptor agonists, and non-steroidal MRAs (e.g., finerenone). Lifestyle modifications and precision medicine approaches further optimize patient outcomes.

Conclusion: The management of diabetic nephropathy requires a multidisciplinary, personalized, and evidence-based approach. Integration of early biomarkers, individualized glycemic and blood pressure control, RAAS inhibition, and new therapeutic agents can significantly delay disease progression and reduce cardiovascular risk. Future directions should

emphasize precision medicine, continued research on novel agents, and collaborative care models to improve long-term outcomes in DN patients.

Keywords: *Diabetic nephropathy, Chronic kidney disease (CKD), SGLT2 inhibitors, Renal biomarkers, Precision medicine*

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Modern approaches to the management of patients with diabetic nephropathy.

This project investigates the current evidence-based approaches for managing patients with diabetes and chronic kidney disease, particularly diabetic nephropathy. It reviews the latest research, clinical guidelines, and other available treatment options.

Project Relevance

Diabetes mellitus and chronic kidney disease represent a major health challenge worldwide, both diseases placing a significant burden on the patients and healthcare workers. CKD is a progressive condition that leads to a decrease in kidney function over time and ultimately results in end-stage renal disease (ESRD). This stage requires renal replacement interventions such as dialysis or, ultimately, kidney transplantation. Currently, an estimated 9-13% adults globally suffer from CKD, and the number of patients with CKD is rising as the incidence of diabetes and hypertension increases in the population.

Diabetic nephropathy is a complication of diabetes associated with chronic kidney disease, and structural and functional alterations in the kidneys characterize it. This includes glomerulosclerosis and increased excretion of albumin in the urine. It increases the risk for developing end-stage renal disease (ESRD) and elevates the chances of cardiovascular complications. According to recent statistical data, diabetes is responsible for ESRD in approximately 40% of CKD patients (Alicic RZ et al., 2017).

Project Objectives

1. To review the epidemiology and pathogenesis of CKD in diabetic patients and understand the main mechanisms connecting these two conditions.
2. To evaluate the current diagnostic methods used in diagnosing and monitoring CKD in diabetic patients, highlighting advancements and challenges.
3. To assess modern treatment approaches, including pharmacological and non-pharmacological strategies, based on the latest clinical studies and trials.
1. To identify future directions for research in this area, including gaps in the literature and emerging treatment techniques.
2. To provide practical recommendations for healthcare practitioners regarding the effective management of these patients.

Project Methodology

1. I will prepare and deliver an informative presentation on the recent developments in diagnosing and managing diabetic nephropathy.
2. I will develop a practical manual on diabetic nephropathy management, outlining diagnostic pathways, therapeutic options, and multidisciplinary strategies.
3. I will request feedback from mentors and collaborators to review the strengths and limitations of the project and refine recommendations for implementation.

Research Methods

The project will employ a comprehensive review of current literature accessed from reputable databases such as PubMed, Cochrane Library, Cureus, Indian Journal of Nephrology, ScienceDirect, Web of Science, and Scopus. These databases provide access to various peer-reviewed articles, systematic reviews, and clinical trials relevant to this topic. Furthermore, additional evidence will be collected from guidelines issued by recognized bodies such as Kidney Disease: Improving Global Outcomes (KDIGO) and the American Diabetes Association (ADA).

Practical Significance

The practical importance of this project lies in its potential to influence patient care and clinical practices directly. This study aims to improve patient outcomes by assessing the latest evidence-based approaches for managing diabetic nephropathy. This project will assist healthcare professionals in delivering high-quality care by addressing gaps in diagnostic methods and management techniques.

Overview of chronic kidney disease and diabetes mellitus:

Chronic Kidney Disease (CKD) and Diabetes Mellitus (DM) are two closely associated conditions that pose a significant public health challenge worldwide. The risk of end-stage renal disease (ESRD) and cardiovascular complications is increased when they present together in the form of diabetic nephropathy (DN).

Epidemiology of Diabetic Nephropathy:

Diabetic nephropathy is one of the significant causes globally of chronic kidney disease and end-stage renal disease, especially in middle—and low-income countries. According to the

International Diabetes Federation (IDF, 2023), approximately 537 million adults worldwide were living with diabetes in 2021; this number is projected to rise to 783 million by 2045.

Burden of diabetic nephropathy: It is increased, especially in developing countries like India, due to the lack of early diagnosis and limited access to specialized care. This contributes to a higher number of patients progressing to ESRD and increases the risk of mortality in these patients. These patients should regularly undergo screening, hospitalizations, and dialysis for the treatment of CKD and diabetes, which increases treatment cost (Keith A. et al., 2021).

Risk Factors of Diabetic Kidney Disease: Multiple risk factors, such as hyperglycemia, hypertension, dyslipidemia, and genetic predisposition, contribute to the development and progression of diabetic nephropathy.

Patients with poorly managed diabetes have persistent hyperglycemia, which in turn causes microvascular damage that affects the renal glomeruli, beginning the pathological changes associated with DN (see Fig. 1) (Cheng D. et al, 2014).

Role of dyslipidemia and obesity: They increase insulin resistance, promote chronic inflammation, and lipid-induced nephrotoxicity, which further accelerates kidney damage. Dyslipidemia plays a role in DKD progression by inducing apoptosis in podocytes, promoting infiltration of macrophages, and stimulating overproduction of extracellular matrix (Hager MR et al, 2016).

Hypertension: As confirmed by a recent meta-analysis, hypertension is a key factor in the onset and progression of diabetic nephropathy. The increased pressure inside glomerular capillaries causes damage to the glomeruli, resulting in proteinuria and ultimately a decrease in kidney function (Wagnew F. et al, 2018).

Pathophysiology of CKD in diabetic patients: The development and progression of diabetic nephropathy are characterized by complex and multifactorial pathogenesis, which is mediated by various pathways.

Traditionally, changes in the renal blood flow are attributed as the underlying mechanism, leading to abnormal hemostasis, including renal ischemia and increased oxidative stress due to changes in glucose metabolism. Along with that, overactivation of the renin-angiotensin-aldosterone system (RAAS) contributes to the progression of DN (Samsu N., 2021).

Hyperglycemia is a key factor: Hyperglycemia leads to dilation of afferent arterioles by releasing mediators, like insulin-like growth factor 1 (IGF-1), nitric oxide (NO), vascular endothelial growth factor (VEGF), glucagon, and prostaglandins. Along with that, in the initial stage of diabetes, changes in the function of renal tubules also occur, and it depends on the patient's glycemic control. The elevated amount of glucose in the filtrate results in upregulation of sodium glucose cotransporter 2 (SGLT2) in the proximal tubules, causing increased reabsorption of sodium and glucose. This reduces sodium chloride availability to the macula densa cells in the distal tubules, which activates tubuloglomerular feedback and causes afferent arteriolar dilation. Simultaneously, efferent arterioles undergo constriction due to elevated angiotensin II levels, leading to disruption in autoregulation and development of glomerular hypertension (see Fig. 2). It has been observed that hyperglycemia, insulin resistance, and compensatory hyperinsulinemia lead to dysfunction of the endothelium, which in turn results in increased production of reactive oxygen species (ROS), activation of protein kinase C (PKC), and pro-inflammatory signalling due to advanced glycation end-product (AGE) accumulation. The oxygen supply to the kidney is impaired by the glomerular and vascular lesions, leading to hypoxia in the renal medulla and dysfunction of the renal tubules. In the later stages of diabetic nephropathy, NO production is decreased in the kidney, diminishing its vasodilative effect. As a compensatory effect, the remaining nephrons' oxygen demand increases. This leads to excessive production of free radicals since there is insufficient supply of oxygen, and thus further exacerbates renal tissue damage (Potenza M. et al, 2011).

Mitochondrial stress: Hyperglycemia leads to mitochondrial stress, producing excessive ROS production, which damages glomerular podocytes and triggers their apoptosis. Furthermore, hyperglycemia and advanced glycation end-products (AGEs) together stimulate production of renin and angiotensinogen in renal cells through the G protein-coupled metabolic receptor GPR91. This activation of the intrarenal renin-angiotensin-aldosterone system (RAAS) accelerates kidney damage. Both transforming growth factor-β1 (TGF-β1) and angiotensin II play an important role in renal tissue fibrosis, which is characterized by tubular dysfunction and renal atrophy. The upregulation of pro-sclerotic growth factors by aldosterone is also believed to play a significant role in the pathophysiology of diabetic nephropathy. The gene expression

changes and macrophage infiltration in the renal tissue further cause renal fibrosis (AlQudah M. et al, 2020).

Current screening and management guidelines for CKD in diabetic patients

Five different stages characterize diabetic nephropathy. Microalbuminuria is the first manifestation detected among patients suffering from this disease. Later, it progresses to macroalbuminuria and renal function decline. The evaluation of albuminuria levels serves as the screening and diagnostic criteria for diabetic nephropathy (see Table 1).

According to the American Diabetes Association (ADA guidelines, 2022), screening to evaluate renal function and urinary albumin levels should be performed at the time of diagnosis for every patient with type 2 diabetes and then conducted yearly thereafter. In contrast, type 1 DM patients should undergo screening after 5 years of initial diagnosis.

Laboratory and imaging assessment of renal function

The most commonly used screening test for identifying early renal damage in patients with diabetes is the urine albumin-to-creatinine ratio (UACR). Albuminuria, characterized by a UACR value of ≥30 mg/g, highlights increased glomerular permeability and is one of the initial markers of diabetic nephropathy. Microalbuminuria, defined as a UACR value between 30 and 300 mg/g, also signifies early kidney damage, whereas macroalbuminuria, with a UACR value of >300 mg/g, is typical of the advanced stage of disease.

Estimated GFR levels. It is crucial for screening and diagnosing chronic kidney disease (Levey AS et al, 2020). The calculation of eGFR is based on serum creatinine levels, along with factors such as age, sex, and race, to assess renal function. An eGFR value more than 90 mL/min/1.73 m^2 is considered normal, whereas values below 60 mL/min/1.73 m^2 signify a substantial decline in renal function and indicate the presence of CKD. It is recommended that annual eGFR screening be done in all diabetic patients to monitor their kidney function effectively (see Fig. 3).

Regular monitoring of serum electrolytes. In CKD patients, it is also important to regularly monitor serum electrolyte levels, including calcium, potassium, and phosphate. The assessment of acid-base analysis is also crucial in these individuals. Since hypertension frequently coexists in patients with diabetes and chronic kidney disease, regular blood pressure monitoring is vital in these individuals. Additionally, these patients need to assess hemoglobin and hematocrit levels since they develop anemia due to underlying kidney disease. The patients suffering from

advanced chronic kidney disease usually develop bone and mineral disorders over time; such individuals should undergo bone density assessment tests like dual-energy X-ray absorptiometry (DEXA) scan or bone density ultrasound (Thomas B., 2019).

Current approaches for the management of diabetic nephropathy

Lifestyle Interventions and Behavioural Modifications. Lifestyle interventions are crucial in preventing kidney disease progression in diabetic patients. Key components include a balanced diet, regular physical exercise, and effective weight control to achieve optimal and stable blood glucose levels.

Low-salt diet. A diet low in salt, free from salty and pickled foods, is strongly recommended for patients with diabetic nephropathy. Low sodium intake is associated with improving blood pressure control, which is an important part of managing chronic kidney disease. It is observed that in patients with diabetes and CKD, consuming increased salt and with albuminuria has a decline in annual creatinine clearance (Hodson EM. et al., 2023).

Low-protein diet. A low-protein diet (LPD), typically defined as protein consumption less than 0.8 g/kg/day, remains a subject of debate in patients with diabetic nephropathy. The primary goal of LPD therapy is to decrease glomerular filtration workload and alleviate uremic symptoms (Zhu H. et al., 2018).

Smoking cessation. In addition to these, smoking cessation in patients with diabetes and chronic kidney disease can significantly reduce its harmful effects on both the renal and cardiovascular systems. Smoking is considered a separate risk factor for the onset of diabetic nephropathy in individuals with type 2 diabetes. Smoking exacerbates vascular damage, accelerates disease progression, and increases the risk of adverse outcomes (Taler SJ et al, 2013)

Pharmacological Management Strategies. Effective blood glucose level control is the cornerstone in preventing and slowing the progression of diabetic nephropathy. The American Diabetes Association (ADA) emphasizes that glycemic control targets should be individualized, taking into account the patient's age, comorbidities, and life expectancy (see Fig. 4).

Metformin. It remains the first-line medication for controlling glycemic levels in patients with type 2 diabetes, including those in the early stages of CKD. However, it should be used cautiously in patients with advanced CKD (eGFR less than 30 mL/min/1.73 m^2) due to the increased risk of lactic acidosis. For patients with advanced stages of CKD, therapy with insulin

or novel agents like SGLT2 inhibitors and GLP-1 receptor agonists should be favoured due to their combined benefits of controlling glucose levels and renoprotective effects (Graham GG et al, 2011)

Sodium-glucose cotransporter-2 (SGLT2) inhibitors. SGLT2 inhibitors such as empagliflozin and canagliflozin are oral hypoglycemic agents that lower blood glucose by reducing glucose uptake in the kidneys, leading to increased urinary glucose excretion.

Glucagon-like peptide 1 (GLP-1) receptor agonists. GLP-1 receptor agonists such as dulaglutide and liraglutide. These drugs mimic the action of the incretin hormone by activating GLP-1 receptors on pancreatic β-cells, which stimulates insulin production, suppresses glucagon secretion, and delays gastric emptying.

Dipeptidyl peptidase-4 (DPP-4) inhibitors. DPP-4 inhibitors, such as sitagliptin and saxagliptin, are a group of glucose-lowering medications that work by inhibiting the DPP-4 enzyme, thereby increasing the levels of endogenous glucagon-like peptide-1 (GLP- 1). This leads to increased insulin secretion while suppressing glucagon secretion.

Optimizing Blood Pressure Control. Hypertension is a significant modifiable risk factor in the worsening of diabetic nephropathy. Achieving optimal and stable blood pressure control is essential for decreasing proteinuria and maintaining renal function. Current guidelines recommend a target BP of <130/80 mmHg in patients with diabetic nephropathy. Adequate blood pressure control helps decrease glomerular hyperfiltration, reduce albuminuria, and slow the decline in GFR, thereby mitigating the progression of renal damage.

Results and interpretation of recent research

Recent research highlights the intricate relation between diabetes and chronic kidney disease, where both conditions exacerbate each other. Additionally, novel biomarkers have shown promise in early diagnosis and improving patient outcomes.

A complex interdependent relationship between diabetes and chronic kidney disease

The complex and interdependent relationship between diabetes mellitus and chronic kidney disease (CKD) is a critical area of focus in the present healthcare system. There are significant clinical complexities involved when a patient presents with both diabetes and renal disease. Managing these coexisting conditions often requires complex treatment strategies to control glycemic levels while preserving renal function effectively (Kumar M. et al, 2023)

Diabetes is a significant risk factor for chronic kidney disease, particularly in the form of diabetic nephropathy. Furthermore, clinical studies have also indicated that chronic kidney disease can contribute to the development or exacerbation of previously stable diabetes (Chen S. et al, 2022). Chronic kidney disease, especially in later stages, can cause impairment in insulin signalling. This disruption can result in insulin resistance, a hallmark sign of type 2 diabetes. Also, there is ineffective glucose uptake in the peripheral tissue, resulting in hyperglycemia, a key symptom of diabetes (Bjornstad P. et al., 2016).

Novel biomarkers for the early diagnosis of diabetic nephropathy

For better outcomes in patients with diabetic nephropathy, it is important to catch the disease process early on.

Cystatin C is an alternative biomarker for assessing GFR that is considered more sensitive than creatinine in the early stage of CKD. All nucleated cells in the body produce Cystatin C protein, which is freely filtered through the renal glomerulus.

Unlike creatinine, Cystatin C is unaffected by the individual's muscle mass; hence, it provides more accurate information about renal function in diabetic patients. It is especially useful in older patients who have reduced muscle mass (Liao X. et al., 2022).

Neutrophil gelatinase-associated lipocalin (NGAL). Another biomarker that can be used for early detection of renal changes is Neutrophil gelatinase-associated lipocalin (NGAL). It is a lipocalin protein present in the tubular cells and released in response to injury to the proximal tubules of the kidney. In diabetic patients, tubular injury usually occurs before glomerular injury; hence, NGAL can be a valuable marker in diagnosing diabetic nephropathy at a very early stage (Kaul A. et al., 2018).

Urinary nephrin is also a promising biomarker for the early detection of diabetic nephropathy. It is found to be elevated even before the appearance of albumin in the urine, highlighting that podocyte injury happens early in the disease process. Assessing urinary nephrin levels can be helpful in patients with normal UACR values. It is a sensitive marker to detect early glomerular damage and podocyte dysfunction.

Furthermore, high levels of urinary nephrin suggest an increased risk of CKD progression and more severe glomerular damage (Kishore K. et al., 2021).

Kidney Injury Molecule-1 (KIM-1). KIM-1, a novel biomarker, is emerging as a promising indicator for early detection of diabetic nephropathy. Under normal conditions, KIM-1 is usually not expressed, but in the case of injury to the proximal tubules, it is upregulated in the epithelial cells of renal tubules. During early kidney damage, KIM-1 can be detected in the urine. This biomarker is ideal for detecting subclinical renal injury, as KIM-1 is positive even before renal function declines. In diabetic patients, urinary KIM-1 precedes albuminuria and is helpful in the early detection of the disease process (Looker HC et al, 2021).

Recommendations

The management of diabetic nephropathy requires a multifaceted approach, integrating lifestyle interventions, pharmacological drugs, and the management of comorbidities. Key strategies include optimizing blood pressure control, utilizing RAAS inhibitors, and controlling target glycemic levels.

Low-protein diet: Some recent studies suggest that LPD therapy may lead to malnutrition due to reduced protein consumption and increased mortality among diseased patients. Current research presents that LPD therapy might not have renoprotective effects, but we still cannot rule out potential benefits of the LPD diet in some patients.

Individualized dietary plans play a key role in deciding to follow a certain diet over others (Cai L. et al., 2024).

Probiotic supplementation: Probiotics have also been shown to slow the progression of kidney injury by enhancing glucose and lipid metabolism, reducing inflammation and thus alleviating oxidative stress in diabetic nephropathy patients (Dai Y. et al, 2022).

Sodium-glucose cotransporter-2 (SGLT2) inhibitors: According to the EMPA-REG outcome study (Empagliflozin Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients), empagliflozin significantly reduced the progression of chronic kidney disease, showing a 39% reduction in adverse outcomes such as cardiovascular death or progressing nephropathy. These findings highlight the dual benefits of using SGLT2 inhibitors in the management of diabetic nephropathy patients (Wanner C. et al, 2016)

Glucagon-like peptide 1 (GLP-1) receptor agonists: GLP-1 receptor agonists have the potential to lower albuminuria and prevent major cardiovascular events in patients with type 2 diabetes and impaired kidney function (GFR < 15 mL/min/1.73 m^2) (de Boer et al, 2022).

Dipeptidyl peptidase-4 (DPP-4) inhibitors: According to recent studies, GLP-1 receptor agonists should be preferred over DPP-4 inhibitors, since GLP-1 receptor agonists have shown potential cardiovascular benefit. Thus, DPP-4 inhibitors should be discontinued in patients with diabetes and CKD (Natale P. et al, 2023).

Blood pressure control: Angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) are the recommended first-line drugs for managing blood pressure and reducing proteinuria. These drugs effectively reduce increased glomerular pressure and lower urinary albumin excretion. The strong recommendation for these drugs is based on extensive research evidence, highlighting that renin-angiotensin-aldosterone system (RAAS) inhibition is the most effective strategy to delay the progression of diabetic nephropathy to end-stage renal disease (Umanath K. et al, 2018).

Treatment of concurrent comorbidities: Along with controlling glycemic levels and hypertension, comorbidities should also be treated to improve the outcome in these patients. The frequently seen comorbidity in patients with diabetes and CKD is dyslipidemia. It is known to increase the progression of CKD and significantly elevates cardiovascular risk. To manage dyslipidemia effectively in these individuals, it is highly recommended to start statin therapy. The evidence from the SHARP trial (Study of Heart and Renal Protection) showed that the combination of lipid-lowering agents such as simvastatin and ezetimibe significantly decreased the occurrence of life-threatening atherosclerotic complications in patients with CKD (Baigent et al, 2011).

Another comorbidity that should be treated simultaneously is anemia. Anemia is a frequent complication found in patients with CKD, especially in patients with diabetic nephropathy. Anemia management typically involves treatment with erythropoiesis-stimulating agents (ESAs) such as epoetin-alfa, alongside iron supplementation, to achieve a target hemoglobin level of 10-12 g/dL. However, it is important to avoid overcorrection of Anemia has been linked to an increased risk of cardiovascular complications (Macdougall et al., 2023).

Patients with diabetes and chronic kidney disease (CKD) frequently experience changes in mineral metabolism, which can result in weakened bone health and calcification of vessels. Effective management strategies involve maintaining phosphate levels through dietary restrictions and phosphate binders. Additionally, supplementation with vitamin D analogs is used

to address secondary hyperparathyroidism. These interventions aim to preserve overall bone health and improve outcomes in this population (Hou YC et al, 2018).

Current challenges and future directions: The complex characteristics of diabetic nephropathy require a multidisciplinary and collaborative care model to manage these patients better and improve patient outcomes. This strategy should involve endocrinologists, nephrologists, cardiologists, and primary care physicians, each addressing specific aspects of the disease. This will likely improve patient outcomes and their quality of life.

Emerging novel drugs and intervention strategies: Finerenone is a non-steroidal mineralocorticoid receptor antagonist (MRA), which has emerged as a promising option for managing diabetic nephropathy due to its renoprotective and cardioprotective effects. Finerenone has shown better receptor selectivity than the traditional steroidal mineralocorticoid receptor antagonists, which minimizes the risk of hyperkalemia and other adverse effects. According to the data from the FIDELIO-DKD trial, finerenone has a remarkable effect on CKD by slowing its progression and lowering adverse cardiovascular events in type 2 diabetic patients and advanced CKD (Bakris GL et al, 2020).

Another class of drugs which has potential in the treatment of diabetic nephropathy is endothelin-1 receptor antagonists (ERAs) such as atrasentan. Endothelin-1 is a potent vasoconstrictor which contributes to glomerular dysfunction and albuminuria. Atrasentan blocks the receptor for endothelin-1, thus reducing proteinuria and slowing the progression of CKD. The recent SONAR study has confirmed the efficacy of atrasentan in reducing the risk of renal events in diabetic patients (Heerspink H. et al, 2019).

Baricitinib, a selective JAK-1 and JAK-2 inhibitor, could be a potential future drug for the management of diabetic nephropathy. It functions by blocking Janus kinase–signal transducer and targets the JAK-STAT signalling pathway, which is responsible for the development of diabetic nephropathy. In recent clinical trials in which participants were

The urinary albumin levels of patients treated with baricitinib were reduced. These findings suggest that JAK inhibitors could emerge as a novel therapy for DN in the future (Tuttle KR et al., 2018).

Ongoing clinical trials: Numerous clinical trials are underway to find novel drugs for managing diabetic nephropathy, which may transform the existing standard of care. Notable among these is

the EMPA-KIDNEY trial, which is evaluating the impact of the SGLT2 inhibitor empagliflozin in patients with CKD, including those without diabetes. The initial findings from this trial suggest that empagliflozin can lead to a significant slowdown in the progression of CKD and decrease cardiovascular complications (EMPA, 2022).

Future directions

In addition, precision medicine offers tailored treatments that take into account patients' unique individual characteristics, such as genetic predispositions and environmental factors. Recent advancements in genetics and molecular biology have opened up new opportunities in identifying novel biomarkers and personalized strategies for diabetic nephropathy.

A significant breakthrough in precision medicine can be observed in managing monogenic diabetes. Treatment for these patients can now be targeted to their specific genetic variant. For example, individuals diagnosed with neonatal diabetes mellitus who exhibit a distinct methylation pattern at the 6q24 chromosomal locus have demonstrated improved glycemic control with sulfonylureas (Downie ML et al, 2023).

Conclusion

Diabetic nephropathy (DN) continues to pose a significant global health challenge, contributing to the widespread prevalence of chronic kidney disease (CKD) and leading to end-stage renal disease (ESRD). The development of diabetic nephropathy is complex and multifactorial, involving factors such as hyperglycemia, oxidative stress, inflammation, and hemodynamic changes that gradually damage the kidney. Diabetes and CKD have an intricate relationship, where each condition exacerbates the other, highlighting the requirement for early detection and comprehensive management strategies.

The diagnostic approaches for diabetic nephropathy have undergone significant advancements, particularly in detecting early biomarkers such as urinary nephrin and kidney injury molecule-1. However, traditional screening methods, including laboratory assessments of renal function and imaging techniques, continue to play a vital role. Prompt diagnosis is essential in the case of diabetic nephropathy for initiating early intervention strategies to delay the progression to advanced CKD.

The management of diabetic nephropathy requires a multifaceted approach integrating lifestyle interventions, pharmacological drugs, and the management of comorbidities. Key strategies

include optimizing blood pressure control, utilizing RAAS inhibitors, and controlling target glycemic levels. Novel therapies such as SGLT2 inhibitors and GLP-1 receptor agonists have also significantly improved renal and cardiovascular outcomes.

Looking ahead, innovative therapies such as non-steroidal mineralocorticoid receptor antagonists (MRAs), JAK-1 and JAK-2 inhibitors, can offer new opportunities to treat the underlying mechanisms of diabetic nephropathy progression. The future of diabetic nephropathy care relies on integrating emerging diagnostic methods, personalized medicine, and a multimodal treatment approach. A collaborative effort among nephrologists,

Endocrinologists and cardiologists are essential for addressing the complexities involved with diabetic nephropathy and improving outcomes among patients.

Reference

Alicic, R. Z., Rooney, M. T., & Tuttle, K. R. (2017). Diabetic kidney disease. *Clinical Journal of the American Society of Nephrology, 12*(12), 2032–2045. https://doi.org/10.2215/CJN.11491116

AlQudah, M., Hale, T. M., & Czubryt, M. P. (2020). Targeting the renin-angiotensin-aldosterone system in fibrosis. *Matrix Biology, 91–92*, 92–108. https://doi.org/10.1016/j.matbio.2020.04.005

American Diabetes Association. (2022). Classification and diagnosis of diabetes: Standards of medical care in diabetes—2022. *Diabetes Care, 45*(Supplement_1), S17–S38. https://doi.org/10.2337/dc22-S002

Baigent, C., Landray, M. J., Reith, C., et al. (2011). The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection). *The Lancet, 377*(9784), 2181–2192. https://doi.org/10.1016/S0140-6736(11)60739-3

Bakris, G. L., Agarwal, R., Anker, S. D., et al. (2020). Effect of finerenone on chronic kidney disease outcomes in type 2 diabetes. *The New England Journal of Medicine, 383*(23), 2219–2229. https://doi.org/10.1056/NEJMoa2025845

Bjornstad, P., Cherney, D. Z., Maahs, D. M., & Nadeau, K. J. (2016). Diabetic kidney disease in adolescents with type 2 diabetes: New insights. *Current Diabetes Reports, 16*(2), Article 11. https://doi.org/10.1007/s11892-015-0708-0

Cai, L., Huang, Y., Li, X., Cao, D., & Liu, F. (2024). Effects of dietary intervention on diabetic nephropathy: An umbrella review of systematic reviews and meta-analyses of randomized controlled trials. *Frontiers in Endocrinology, 15*. https://doi.org/10.3389/fendo.2024.1385872

Chen, S., Chen, L., & Jiang, H. (2022). Prognosis and risk factors of chronic kidney disease progression in patients with diabetic kidney disease and non-diabetic kidney disease: A prospective cohort CKD-ROUTE study. *Renal Failure, 44*(1), 1309–1318. https://doi.org/10.1080/0886022X.2022.2106872

Cheng, D., Fei, Y., Liu, Y., et al. (2014). HbA1C variability and the risk of renal status progression in diabetes mellitus: A meta-analysis. *PLOS ONE, 9*(12), e115509. https://doi.org/10.1371/journal.pone.0115509

Dai, Y., Quan, J., Xiong, L., Luo, Y., & Yi, B. (2022). Probiotics improve renal function, glucose, lipids, inflammation and oxidative stress in diabetic kidney disease: A systematic review and meta-analysis. *Renal Failure, 44*(1), 862–880. https://doi.org/10.1080/0886022X.2022.2079522

De Boer, I. H., Khunti, K., Sadusky, T., et al. (2022). Diabetes management in chronic kidney disease: A consensus report by the American Diabetes Association (ADA) and Kidney Disease: Improving Global Outcomes (KDIGO). *Diabetes Care, 45*(12), 3075–3090. https://doi.org/10.2337/dci22-0027

Downie, M. L., Desjarlais, A., Verdin, N., Woodlock, T. J., & Collister, D. (2023). Precision medicine in diabetic kidney disease: A narrative review framed by lived experience. *Canadian Journal of Kidney Health and Disease, 10*, 20543581231209012. https://doi.org/10.1177/20543581231209012

Graham, G. G., Punt, J., Arora, M., et al. (2011). Clinical pharmacokinetics of metformin. *Clinical Pharmacokinetics, 50*(2), 81–98.

Hager, M. R., Narla, A. D., & Tannock, L. R. (2016). Dyslipidemia in patients with chronic kidney disease. *Reviews in Endocrine and Metabolic Disorders, 18*(1), 29–40. https://doi.org/10.1007/s11154-016-9402-z

Heerspink, H. J. L., Parving, H. H., Andress, D. L., et al. (2019). Atrasentan and renal events in patients with type 2 diabetes and chronic kidney disease (SONAR): A double-blind, randomised, placebo-controlled trial. *The Lancet, 393*(10184), 1937–1947. https://doi.org/10.1016/S0140-6736(19)30772-X

Hodson, E. M., & Cooper, T. E. (2023). Altered dietary salt intake for preventing diabetic kidney disease and its progression. *Cochrane Database of Systematic Reviews, 2023*(1), CD006763. https://doi.org/10.1002/14651858.CD006763.pub3

Hou, Y. C., Lu, C. L., & Lu, K. C. (2018). Mineral bone disorders in chronic kidney disease. *Nephrology, 23*, 88–94. https://doi.org/10.1111/nep.13457

International Diabetes Federation. (2023). *Diabetes facts & figures*. https://idf.org/about-diabetes/diabetes-facts-figures/

Kaul, A., Behera, M., Rai, M., et al. (2018). Neutrophil gelatinase-associated lipocalin: As a predictor of early diabetic nephropathy in type 2 diabetes mellitus. *Indian Journal of Nephrology, 28*(1), 53–58. https://doi.org/10.4103/ijn.IJN_96_17

Keith, A., Betts, P., Song, J., Faust, E., et al. (2021). Medical costs for managing chronic kidney disease and related complications in patients with chronic kidney disease and type 2 diabetes. *The American Journal of Managed Care, 27*(20). https://www.ajmc.com/view/medical-costs-for-managing-chronic-kidney-disease-and-related-complications-in-patients-with-chronic-kidney-disease-and-type-2-diabetes

Kishore Kondapi, N., Lakshmana Kumar, N., Moorthy, S., & Silambanan, S. (2021). A study of association of urinary nephrin with albuminuria in patients with diabetic nephropathy. *Indian Journal of Nephrology, 31*(2), 142. https://doi.org/10.4103/ijn.IJN_305_19

Kumar, M., Dev, S., Khalid, M. U., et al. (2023). The bidirectional link between diabetes and kidney disease: Mechanisms and management. *Cureus, 15*(9), e45615. https://doi.org/10.7759/cureus.45615

Levey, A. S., Eckardt, K. U., Dorman, N. M., et al. (2020). Nomenclature for kidney function and disease—Executive summary and glossary from a Kidney Disease: Improving Global Outcomes (KDIGO) consensus conference. *European Heart Journal, 41*(48), 4592–4598. https://doi.org/10.1093/eurheartj/ehaa650

Liao, X., Zhu, Y., & Xue, C. (2022). Diagnostic value of serum cystatin C for diabetic nephropathy: A meta-analysis. *BMC Endocrine Disorders, 22*(1), Article 145. https://doi.org/10.1186/s12902-022-01052-0

Looker, H. C., Colombo, M., Hess, S., et al. (2015). Biomarkers of rapid chronic kidney disease progression in type 2 diabetes. *Kidney International, 88*(4), 888–896. https://doi.org/10.1038/ki.2015.199

Macdougall, I. C. (2023). Anaemia in CKD – Treatment standard. *Nephrology, Dialysis, Transplantation*. Advance online publication. https://doi.org/10.1093/ndt/gfad250

Natale, P., Palmer, S. C., Tunnicliffe, D. J., Toyama, T., & Strippoli, G. F. M. (2023). Dipeptidyl peptidase 4 (DPP-4) inhibitors for people with chronic kidney disease and diabetes. *Cochrane Database of Systematic Reviews, 2023*(8), CD015906. https://doi.org/10.1002/14651858.CD015906

Potenza, M., Gagliardi, S., Nacci, C., Carratu, M., & Montagnani, M. (2011). Endothelial dysfunction in diabetes. *Current Medicinal Chemistry, 16*(1), 94–112. https://doi.org/10.2174/092986709787002853

Samsu, N. (2021). Diabetic nephropathy: Challenges in pathogenesis, diagnosis, and treatment. *BioMed Research International, 2021*, Article 1497449. https://doi.org/10.1155/2021/1497449

Taler, S. J., Agarwal, R., Bakris, G. L., et al. (2013). KDOQI US commentary on the 2012 KDIGO clinical practice guideline for management of blood pressure in CKD. *American Journal of Kidney Diseases, 62*(2), 201–213. https://doi.org/10.1053/j.ajkd.2013.03.018

The EMPA-KIDNEY Collaborative Group. (2022). Empagliflozin in patients with chronic kidney disease. *New England Journal of Medicine, 388*(2), 117–127. https://doi.org/10.1056/NEJMoa2204233

Thomas, B. (2019). The global burden of diabetic kidney disease: Time trends and gender gaps. *Current Diabetes Reports, 19*(4), Article 18. https://doi.org/10.1007/s11892-019-1133-6

Tuttle, K. R., Brosius, F. C., Adler, S. G., et al. (2018). JAK1/JAK2 inhibition by baricitinib in diabetic kidney disease. *Nephrology, Dialysis, Transplantation, 33*(11), 1950–1959. https://doi.org/10.1093/ndt/gfx377

Umanath, K., & Lewis, J. B. (2018). Update on diabetic nephropathy: Core curriculum 2018. *American Journal of Kidney Diseases, 71*(6), 884–895. https://doi.org/10.1053/j.ajkd.2017.10.026

Wagnew, F., Eshetie, S., Kibret, G. D., et al. (2018). Diabetic nephropathy and hypertension in diabetes patients of sub-Saharan countries: A systematic review and meta-analysis. *BMC Research Notes, 11*(1), 565. https://doi.org/10.1186/s13104-018-3670-5

Wanner, C., Inzucchi, S. E., Lachin, J. M., et al. (2016). Empagliflozin and progression of kidney disease in type 2 diabetes. *New England Journal of Medicine, 375*(4), 323–334. https://doi.org/10.1056/NEJMoa1515920

Zhu, H., Jiang, Z., Gong, P., et al. (2018). Efficacy of low-protein diet for diabetic nephropathy: A systematic review of randomized controlled trials. *Lipids in Health and Disease, 17*(1), 141. https://doi.org/10.1186/s12944-018-0791-8

Tables

Table 1: Albuminuria criteria in diabetic nephropathy

Normoalbuminuria	Daily urine albumin amount is less than 30 mg
Microalbuminuria	Daily urine albumin amount is in between 30 mg–300 mg or Ratio of urine albumin by urine creatinine is 30–300
Macroalbuminuria	Daily urine albumin amount is greater than 300 mg or Ratio of urine albumin by urine creatinine is greater than 300

Special journal of the Medical Academy and other Life Sciences
Vol. 3 No. 5 (2025)

Figures

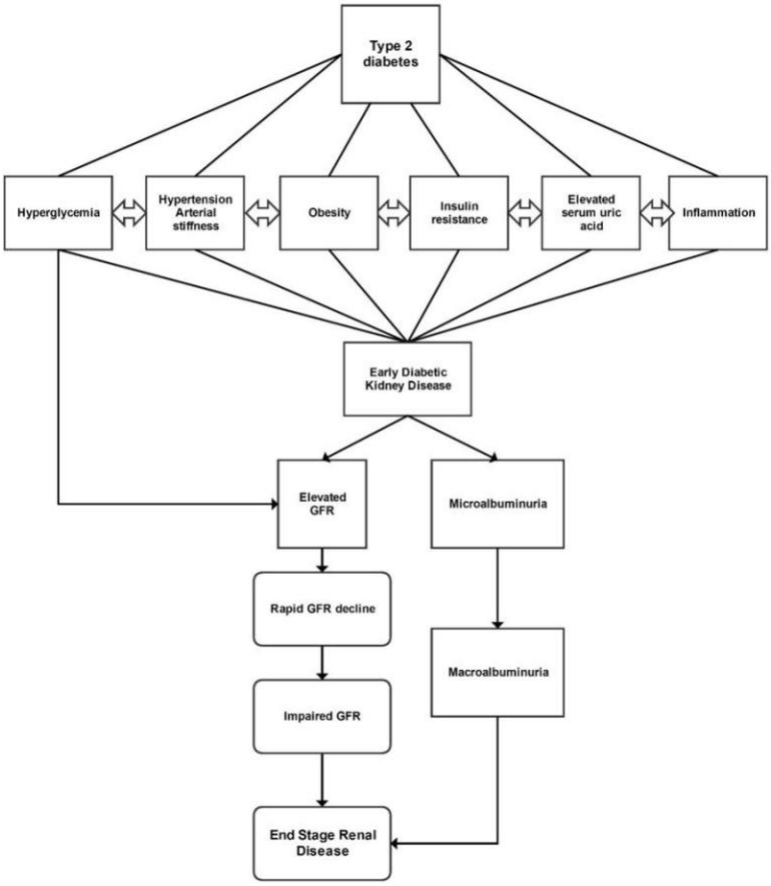


Figure 1. Risk factors for diabetic nephropathy with type 2 diabetes

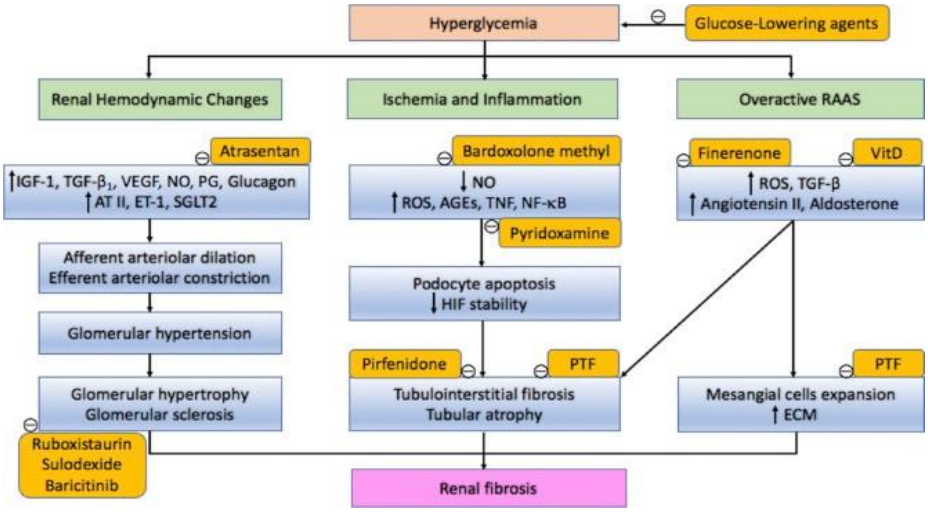
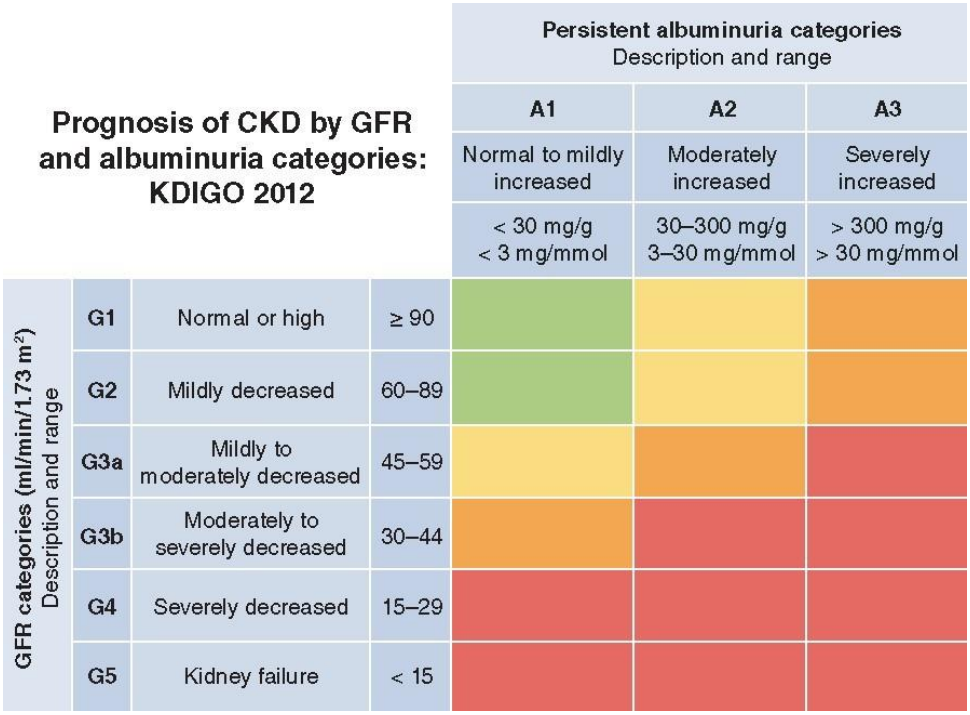


Figure 2. Pathophysiology of diabetic kidney disease



Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				< 30 mg/g < 3 mg/mmol	30–300 mg/g 3–30 mg/mmol	> 300 mg/g > 30 mg/mmol
GFR categories (ml/min/1.73 m²) Description and range	G1	Normal or high	≥ 90			
	G2	Mildly decreased	60–89			
	G3a	Mildly to moderately decreased	45–59			
	G3b	Moderately to severely decreased	30–44			
	G4	Severely decreased	15–29			
	G5	Kidney failure	< 15			

Figure 3. Kidney Disease: Improving Global Outcomes (KDIGO) classification for CKD

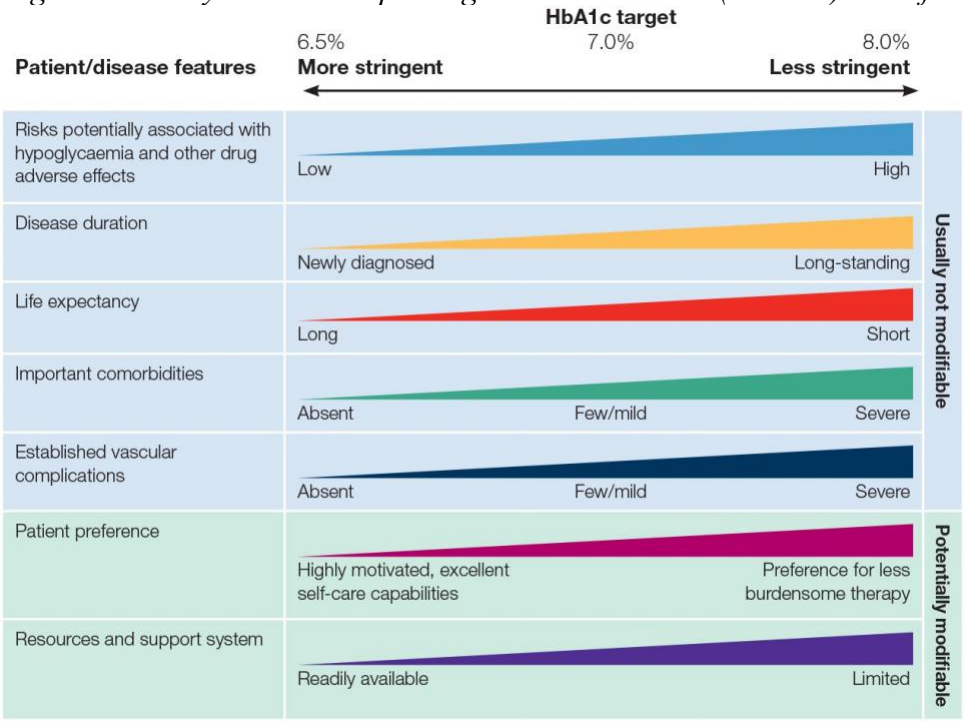


Figure 4. Several key patient characteristics that should be taken into consideration when personalizing HbA1c targets are outlined on the left.