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Risk Factors for Diabetic Nephropathy: A Comprehensive Review

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Abstract: India will be severely affected due to rise in diabetes incidence up to 6.6 million cases of diabetic nephropathy who are expected in the country which will be draining huge treatment cost (Shobhana et al, 2000). Diabetic nephropathy (DN) is a major micro vascular complication of diabetes mellitus (DM) and a leading cause of end-stage renal disease (ESRD) globally. This review explores the multifactorial risk factors associated with the development and progression of DN, including hyperglycemia, hypertension, genetic predisposition, dyslipidemia, smoking, obesity, and duration of diabetes. Early identification of these factors is essential for preventive strategies and delaying the progression of renal damage in diabetic patients.

Key words: hypertension, Diabetic Nephropathy, diabetes incidence, micro vascular complication

Introduction- India being the most populous country is likely to become the hub of diabetic patients and subsequently of diabetic nephropathy. Diabetes consequently diabetic nephropathy drains a huge amount on treatment expenditure. Increased incidence of diabetes has led to increased kidney dysfunction. Diabetic nephropathy is a chronic kidney disease characterized by persistent albuminuria, progressive decline in glomerular filtration rate (GFR), and increased cardiovascular morbidity and mortality. It affects nearly 30–40% of individuals with type 1 or type 2 diabetes mellitus (American Diabetes Association [ADA], 2022). Understanding the risk factors contributing to DN is crucial for early diagnosis and effective disease management. Patient should keep their blood glucose and blood pressure as close to normal by preventive measures such as balanced diet taking medicines and doing regular exercise.

2. Pathophysiology of Diabetic Nephropathy- DN results from complex metabolic and hemodynamic disturbances triggered by chronic hyperglycemia. Key mechanisms include glomerular hyperfiltration, increased oxidative stress, inflammation, and activation of the renin-angiotensin-aldosterone system (RAAS), which collectively lead to glomerulosclerosis and tubulointerstitial fibrosis.

3. Risk Factors-

3.1. Hyperglycemia: Persistent hyperglycemia is the most significant risk factor for DN. High blood glucose levels promote the formation of advanced glycation end-products (AGEs), activate protein kinase C (PKC), and up regulate pro-inflammatory cytokines, resulting in structural and functional renal changes. Hyperglycemia has been found to be a major factor in progression of diabetic nephropathy

3.2. Hypertension: Hypertension accelerates the progression of DN by increasing glomerular capillary pressure, leading to endothelial dysfunction and further damage to renal tissues. Blood pressure control is critical, with guidelines recommending a target of <130/80 mmHg for diabetic patients with nephropathy. Proteinuria gets increased in the condition of uncontrolled hypertension (Sarafidis et al, 2007). It ranks among the most relevant progression to promote nephropathy (Jacobson, 1991).

3.3. Duration of Diabetes: The likelihood of developing DN increases with the duration of diabetes. In type 1 diabetes, nephropathy typically develops after 5–10 years of disease onset, whereas in type 2 diabetes, it may be present at diagnosis due to delayed detection.

3.4. Genetic Predisposition: Family history of DN and certain genetic polymorphisms (e.g., ACE gene I/D polymorphism) have been associated with increased susceptibility, indicating a heritable component in DN risk.

3.5. Dyslipidemia: Dyslipidemia also plays an important role in the pathophysiology and progression of vascular disease and probably diabetic nephropathy as well (Austin et al, 1990). Elevated triglycerides and low high-density lipoprotein (HDL) levels contribute to endothelial damage and glomerular injury. Lipid abnormalities are commonly seen in diabetic patients with nephropathy and may be both a cause and consequence of renal dysfunction. Hyperlipidemia is a risk factor for more rapid decline in GFR and increased mortality (Samulsson et al, 1993).



3.6. Obesity: Obesity contributes to insulin resistance and glomerular hyperfiltration, promoting renal injury. Adipose tissue also secretes inflammatory cytokines that exacerbate kidney damage. In a large retrospective cohort study of over 300,000 adults there was a strong and graded independent relationship between BMI and risk for kidney failure (Hsu, et al, 2006).

3.7. Smoking: Smoking in the progression of diabetic nephropathy, a major micro vascular complication of diabetes mellitus Smoking worsens microvascular complications of diabetes, including DN. It promotes oxidative stress and endothelial dysfunction, accelerating renal decline. People who smoke regularly or consume tobacco and are diabetic tend to experience an earlier onset of nephropathy. Smoking act as fuel tank in the progression of diabetic nephropathy (Chakkarwar, V.A. (2012).

4. Diagnosis and Biomarkers- The earliest clinical indicator of DN is microalbuminuria (30–300 mg/day). Persistent macroalbuminuria (>300 mg/day) indicates more advanced disease. Estimated GFR, serum creatinine, and biomarkers such as cystatin C are used to monitor renal function.

5. Prevention and Management- Early intervention focusing on glycemic control (HbA1c <7%), blood pressure regulation, RAAS blockade (ACE inhibitors or ARBs), lifestyle modification (diet, exercise, smoking cessation), and lipid control can significantly delay progression. Novel therapies such as SGLT2 inhibitors and GLP-1 receptor agonists show promise in renoprotection.

6. Discussion- The interplay of modifiable and non-modifiable risk factors in DN emphasizes the importance of individualized patient care. While hyperglycemia and hypertension remain pivotal, emerging data highlight the roles of genetics, inflammation, and lifestyle factors. Screening and targeted interventions must begin early, especially in high-risk groups.

Conclusion- Diabetic nephropathy is a preventable but serious complication of diabetes. The development of diabetic nephropathy are influenced by metabolic, genetic and lifestyle factors. Early identification of risk factors especially glycemic control, blood pressure, smoking cessation and weight management are essential in preventing renal complications in patients with diabetes. Recognizing and managing the risk factors early can mitigate disease burden. Multidisciplinary approaches and patient education are key to successful outcomes.

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