THE ORIGIN OF CHRONIC KIDNEY DISEASE IN PATIENTS WITH DIABETES

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Abstract. *Chronic kidney disease (CKD) is increasingly recognized as a global health issue and it affects 10% to 15% of the world population. Diabetes mellitus is the leading cause of end-stage renal disease. More than 422 million adults in the world populations are living with diabetes mellitus, 40% of whom will develop CKD. Chronic kidney disease is a common complication and concomitant condition of diabetes mellitus. The treatment of patients with diabetes and chronic kidney disease, including intensive control of blood sugar and blood pressure, has been very similar for type 1 and type 2 diabetes patients. New therapeutic targets have shown promising results and may lead to more specific treatment options for patients with type 1 and type 2 diabetes.*

Keywords: *renal disease, diabetes mellitus, diabetic nephropathy.*

ПРОИСХОЖДЕНИЕ ХРОНИЧЕСКОЙ БОЛЕЗНИ ПОЧЕК У ПАЦИЕНТОВ С ДИАБЕТОМ

Аннотация. *Хроническая болезнь почек (ХБП) все чаще признается глобальной проблемой здравоохранения и затрагивает от 10% до 15% населения мира. Сахарный диабет является основной причиной терминальной стадии почечной недостаточности. Более 422 миллионов взрослых в мире живут с сахарным диабетом, у 40% из которых разовьется ХБП. Хроническая болезнь почек является распространенным осложнением и сопутствующим состоянием сахарного диабета. Лечение пациентов с диабетом и хронической болезнью почек, включая интенсивный контроль уровня сахара в крови и артериального давления, было очень похожим для пациентов с диабетом 1-го и 2-го типов. Новые терапевтические цели показали многообещающие результаты и могут привести к более специфическим вариантам лечения для пациентов с диабетом 1-го и 2-го типов.*

Ключевые слова: *болезнь почек, сахарный диабет, диабетическая нефропатия.*

Worldwide, diabetes mellitus (DM) is a growing healthcare challenge and imposes a heavy burden on public health. DM type 2 accounts for more than 90% of diabetes cases, and there is a rising number of people diagnosed with diabetes type 2 with more rapid increase in low- and middle-income countries than in high-income countries.

The World Health Organization estimates that, globally, 422 million adults older than age 18 years (8.5% of the world adult population) were living with diabetes in 2014.

More than 40% of people with diabetes will develop CKD and a significant number will develop ESRD, requiring renal replacement therapies. It estimated that by the year 2030, more than 70% of patients with ESRD will be residents of developing countries. Patients with both diabetes and CKD are at higher risk of cardiovascular morbidities and mortality, kidney failure, and death when compared with those without CKD. Diabetic kidney disease (DKD) is a major long-term complication of DM type 2 and is the leading cause of chronic kidney disease (CKD) and end-stage kidney disease (ESKD) worldwide. Although renal biopsy is the gold standard to diagnose diabetic nephropathy, the majority of diabetic patients do not undergo kidney biopsy, as they are presumed to have diabetic kidney disease based upon clinical history and laboratory evaluation and because of invasive nature of kidney biopsy. Furthermore, an increasing number of DM type 2 patients present with DKD. The incidence and rate of DKD are less clear in DM type 2 than in type 1, mainly due to the highly variable age of onset and difficulty in defining the exact time of onset and associated comorbidities.

Type 1 and type 2 diabetes mellitus can both cause longterm microvascular and macrovascular complications, contributing to the increased morbidity and mortality among these patients. Kidney disease in patients with diabetes can be a result of microvascular complications from diabetes, a concomitant kidney disease of other origin or a combination of the two. In type 1 diabetes patients, microvascular disease secondary to diabetes is the most common etiology to chronic kidney disease, while a spectrum of etiologies can cause kidney disease in type 2 diabetes patients.

Chronic kidney disease and type 1 diabetes mellitus

Type 1 diabetes mellitus (T1D) is a chronic autoimmune condition in which the body's immune system mistakenly attacks and destroys the insulin-producing cells in the pancreas, known as beta cells. Type 1 diabetes usually affects young and middle-aged patients and among these patients, chronic kidney disease is most often caused by diabetes-related microvascular disease (3), a condition which has been referred to as diabetic nephropathy or 'diabetic kidney disease' in the literature.

Chronic kidney disease (CKD) is a common and serious complication that can develop after many years of living with Type 1 diabetes mellitus (T1D). This condition is often referred to as **diabetic nephropathy** when it occurs in people with diabetes. Diabetic nephropathy is a form of kidney damage that can result from high blood sugar levels over time, which damage the blood vessels in the kidneys. In Type 1 diabetes, prolonged high blood sugar levels can damage the small blood vessels in the kidneys, impairing their ability to filter waste from the blood. This damage can progress in stages and lead to kidney failure if not managed properly.

Chronic kidney disease in type 1 diabetes patients is initially characterized by hyperfiltration due to increased glomerular filtration pressure. Cherney et al. postulated hyperglycaemia-dependent hyperfiltration to be mediated through upregulated backtransportation of sodium and glucose from the renal tubular system. Sodium-glucose-co-transporter-2 (SGLT2) contributes to 90% of this transportation reducing distal tubular flux of glucose and sodium. Due to reduced sodium flux in the loop of Henle, macula densa signals dilatation of the afferent arteriolar tone through a tubuloglomerular feedback mechanism which increases tubular sodium flux at the expense of increase of intraglomerular pressure and hyperfiltration at the nephron level.

Hyperfiltration is in the clinic seen as an increase in glomerular filtration rate (GFR).

Albuminuria and hypertension subsequently occur as the kidney disease develops. After the initial hyperfiltration phase, nephrons are lost resulting in a steady GFR decline ranging 3–6 mL/min/year. Renal failure requiring replacement therapy may eventually occur within 20–25 years. During this process, the remaining nephrons compensate by hyperfiltration not only due to hyperglycemia but now also due to reduced total filtration surface. This represents a vicious circle with progressive loss of nephrons.

Chronic kidney disease and type 2 diabetes mellitus

Type 2 diabetes mellitus (T2D**)** is a chronic condition that affects the way your body processes blood sugar (glucose). Unlike Type 1 diabetes, where the body doesn't produce insulin, Type 2 diabetes is characterized by insulin resistance—meaning the body's cells don't respond properly to insulin. Over time, the pancreas can't produce enough insulin to maintain normal blood sugar levels.

While chronic kidney disease in type 1 diabetes most often is secondary to diabetes microvascular disease, there is a whole spectrum of chronic kidney disease etiologies in type 2 diabetes. Type 2 diabetes patients are often older at the time of diagnosis and kidney disease due to other causes than diabetes is likely to occur. Several studies have verified that kidney disease in type 2 diabetes may be a more compounded entity than what is seen in type 1 diabetes.

Regardless of kidney disease etiology, strict blood glucose control is on a group level the single-most important intervention to prevent kidney disease to develop in patients with type 1 and type 2 diabetes. Normalization of blood glucose might act renoprotective through different mechanisms: reduced hyperfiltration on the nephron level, reduced generation of toxic intermediates such as reactive oxygen species (ROS) and reduced activity in pathogenetic signalling pathways including the polyol, hexasamine, protein kinase C and advanced glycation end-product pathways.

Diagnosis of chronic kidney disease in patients with diabetes

The diagnosis of chronic kidney disease (CKD**)** in patients with **diabetes** involves a combination of clinical evaluation**,** laboratory tests**,** and monitoring for early signs of kidney damage**.** Since diabetes, particularly **Type 1** and **Type 2 diabetes**, is one of the leading causes of CKD, regular screening for kidney function is important for early detection and intervention.

Screening for Early Signs of Kidney Damage**:**

1.Urine albumin-to-creatinine ratio (UACR): The most common screening test to detect kidney damage is the urine albumin-to-creatinine ratio (UACR). Elevated levels of **albumin** (a type of protein) in the urine indicate kidney damage. Normal UACR is typically less than 30 mg/g, and values above 30 mg/g suggest **microalbuminuria** (early kidney damage).

-Microalbuminuria (30-300 mg/g): Early signs of kidney damage.

-Macroalbuminuria (greater than 300 mg/g): More severe damage or progression to kidney disease.

2.Urine dipstick test: This is a quick test for the presence of protein (albumin) in the urine, though it is less sensitive than UACR. Proteinuria (protein in the urine) is a sign of kidney dysfunction.

Assessing Kidney Function with Blood Tests**:**

1.Serum creatinine: This test measures the level of creatinine (a waste product) in the blood. High creatinine levels can indicate impaired kidney function because the kidneys normally filter it out. However, creatinine levels can be influenced by other factors, such as muscle mass, so it’s not the most accurate measure of kidney function on its own.

2.Estimated Glomerular Filtration Rate (eGFR): The eGFR is a calculated value based on the serum creatinine level, age, sex, and race. It estimates how well the kidneys are filtering waste from the blood. A **normal eGFR** is usually 90 mL/min/1.73 m² or higher, while an eGFR below 60 mL/min/1.73 m² for at least three months suggests CKD.

Assessing the Presence of Other Kidney Damage Indicators:

-**Blood pressure**: High blood pressure (hypertension) is common in patients with diabetes and is both a cause and consequence of kidney damage. Hypertension can accelerate the progression of CKD.

-**Retinal examination**: Since diabetic retinopathy (damage to the eyes' blood vessels) is common in patients with diabetes, an eye exam can sometimes reveal clues about kidney involvement, as both the eyes and kidneys are affected by similar vascular damage.

Imaging Studies:

-**Ultrasound**: A kidney ultrasound can be performed to assess the size and structure of the kidneys, looking for abnormalities such as cysts, scarring, or other changes typical of kidney disease.

-CT scans or MRIs: These are used less frequently but may be helpful for diagnosing complications or other causes of kidney disease.

Conclusion: Diabetic kidney disease (DKD) is a major long-term complication of diabetes mellitus (DM). Our study demonstrated that approximately one half of patients with type 2 DM had DKD. Further studies are necessary to understand this high prevalence and the underlying factors.

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