



## FREQUENCY AND RISK FACTORS OF DIABETIC NEPHROPATHY (LITERATURE REVIEW)

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**Annotation:** Diabetic nephropathy (DN) is the leading cause of disability and mortality in patients with diabetes mellitus (DM). Developing in 40-45% of patients with both insulin-dependent - IDDM (type I) and insulin-independent - NIDDM (type II) DM, this formidable complication leads to the development of chronic renal failure, and ultimately to the death of patients from uremia. The atogenesis of the development of DN is complex and has its own characteristics. This problem has not lost its relevance at the present time. The treatment of already the last stage of DN is not only a complex process, but also, due to some economic aspects, very costly. It is much easier to deal with the prevention of vascular complications and try to prevent the transition of the disease to the end stage of renal failure than to treat patients with CRF by hemodialysis.

**Keywords:** diabetes mellitus, diabetic nephropathy, albuminuria, hyperglycemia, arterial hypertension, hyperlipidemia.

### Introduction

At present, diabetes mellitus (DM) occupies one of the first places in terms of the severity of complications and mortality due to this disease, and the prevalence of diabetes and its vascular complications is rampant [4, 7, 15, 17].

WITH Diabetes mellitus is a global problem that has only grown over the years. According to the International Diabetes Federation, more than 425 million people worldwide suffer from this disease, most of them are patients with type 2 diabetes. The saddest thing is that every second of them does not even suspect about his illness. After all, as you know, diabetes can develop imperceptibly for many years, without causing any symptoms.

Experts note that in developed countries the number of diabetics is doubling every 15 years, and this increase has not yet been stopped. According to forecasts, by 2040 the number of diabetics will reach 642 million and 540 thousand of them will be children under 14 years of age. Due to the severity of this problem, WHO has declared diabetes mellitus an epidemic of the 21st century.[20]. The greatest danger of diabetes, of course, is associated with complications that develop due to its damaging effect on blood vessels.

An important place in this series is occupied by diabetic nephropathy (DN), which develops in approximately 20.1%, of patients with type 1 DM and 6.3% of patients with type 2 DM [3].

The main cause of end-stage chronic kidney disease, both in Europe and in the USA and Japan, is nephropathy associated with type 2 diabetes [12].

In diabetic nephropathy, arterioles, arteries, glomeruli and tubules of the kidneys are affected [10, 11, 12, 13]. DN is characterized by damage to the tissues of the kidneys in diabetes mellitus, which leads





to the development of diffuse or nodular glomerulosclerosis, which, in turn, leads to the development of chronic renal failure (CRF).

### **Risk Factors for Diabetic Nephropathy**

Diabetic nephropathy develops under the influence of a huge number of reasons. But of the whole variety of mechanisms for the development of DN, the most studied and proven are: *metabolic* (hyperglycemia, hyperlipidemia) and *hemodynamic* (intraglomerular hypertension, arterial hypertension (AH)).

**Hyperglycemia.** hyperglycemia occupies a leading role in the development of micro- and macrovascular complications. It induces non-enzymatic protein glycation, oxidative stress, activates protein kinase C, mitogen-activating protein kinase, the action of growth factors, vasoactive factors, cytokines that cause kidney damage at the cell level. This leads to the development of renal hypertrophy and the accumulation of extracellular matrix, which precede such irreversible changes as glomerulosclerosis and tubulointerstitial fibrosis [2,5,7].

I.I. Dedov et al. studied prognostic factors that determine the risk of progression of DN in individuals with type 1 and type 2 diabetes with a disease duration of more than 20 years [7,15,17]. It has been established that an independent risk factor for the development of microalbuminuria in type 1 and type 2 diabetes is also the level of HbA1c [7]. As noted in international recommendations, at any stage of DN it is necessary to achieve an individual target level of HbA1c in the range of 6.5–7.0%, which reduces the risk of development and progression of DN in both types of DM. According to the provisions of the NKF KDOQI (National Kidney Foundation-Kidney Disease Outcomes Quality Initiative), to prevent the development and progression of microvascular complications, including DN, the HbA1c value should be less than 7.0%. Although the relationship with the quality of glycemic control is lost when DN progresses to the stage of renal failure,

To date, there is no doubt about the need to achieve optimal glycemic control to prevent the development and increase in the severity of DN.

**Hyperlipidemia.** It is known that, along with chronic hyperglycemia, lipid metabolism disorders are risk factors for the development and progression of DN. The above study highlights the role of hyperlipidemia in the development of DN. In Uzbekistan, Urgench, among the unorganized male and female population aged 40-59 years, the frequency of DLP was: HCS - 9.8%, HTG - 9.9%, hypoalphacholesterolemia - 9.2% [8,14,26]. In Tashkent, HCH, HTG and hypoalphacholesterolemia occur in 9.7%, 4.3% and 12.6% of women aged 20-59, respectively. Moreover, starting from the age group of 30-39 years, there is a significant increase in these indicators [14].

Patients with DM have complex lipid disorders: reduced levels of high-density lipids (HDL), elevated levels of triglycerides (TG), low-density lipids (LDL), which are especially pronounced in DN.

The existence of a complete analogy between the process of formation of glomerulosclerosis and atherosclerotic plaque of the vascular wall has been established [10,12]. This is facilitated by the structural similarity of the mesangial cells of the glomeruli with the smooth muscle cells of the arteries. Oxidized LDL, growth factors and cytokines increase the synthesis of mesangial matrix components, accelerating glomerular sclerosis. In addition, lipids filtered into the primary urine can also damage the cells of the renal tubules.

**Proteinuria** most often considered as the most important non-hemodynamic predictor of the progression of DN. When the structure of the renal filter is disturbed, large molecular proteins come





into contact with the mesangium and with the cells of the renal tubules, which leads to toxic damage to the mesangial cells, accelerated sclerosis.

Glomerular formation, the development of an inflammatory process in the interstitial tissue. According to some data, the prevalence of albuminuria in type 2 diabetes is 43.5% [13,16]. Persistent albuminuria leads to pronounced structural changes in the glomeruli. As a rule, at this stage, proteinuria and a decrease in GFR are often recorded as an indicator of the formation of glomerulosclerosis [18].

According to the researchers, the development of renal failure against the background of nephrotic syndrome, especially with changes in the fundus and the absence of an active urinary syndrome, can be considered a characteristic manifestation of DN. The most regular detection of interstitium fibrosis in patients with diabetes with proteinuria and renal failure [16,18].

**Arterial hypertension.** The prevalence of arterial hypertension (AH) among the population of the Russian Federation is 40-45%. Among the population of women aged 40-49 years in Urgench (Uzbekistan), the prevalence of hypertension was 17.6%. When studying the prevalence of hypertension among the male population aged 20-69 years in Tashkent, it was found that hypertension in this age range occurs at a frequency of 17.13% [9].

It should be noted that if in type 1 DM the frequency of AH was 10–30%, then in type 2 DM this figure reached 60–80%. In patients with type 2 diabetes, primary hypertension in 80% of cases precedes the development of diabetes. On the contrary, in persons with hypertension, the frequency of type 1 DM was 2.43 times higher than in normotensive patients. There is also evidence that the number of people with hypertension in the world by 2025 may approach 1.6 billion [1].

Arterial hypertension plays a key role in the development and progression of DN, as well as in the development of macrovascular pathology. As DN progresses, the role of metabolic factors decreases, and the role of hemodynamic factors (AH, intraglomerular hypertension) increases. It is possible to prevent the development and progression of vascular complications (including DN) only if blood pressure is maintained at a level of no more than 130/80

mm. rt. Art. Tighter control of blood pressure in individuals with renal pathology may lead to hypoperfusion of other target organs [6,10,13].

Arterial hypertension and DM are interrelated pathologies that have a powerful mutually reinforcing damaging effect directed at several target organs at once [10,27]. Earlier review studies have shown that mesangial cells are activated in AH, as evidenced by the expression of smooth muscle  $\alpha$ -actin (SMA) [10]. With prolonged AH, the activity of mesangial cells decreases, which is accompanied by a decrease in SMA expression and the disintegration of glomerular loops.

In turn, in the progression of DN there is such a hemodynamic factor as intraglomerular hypertension, that is, increased pressure in the capillaries of the renal glomeruli. Of course, the renin-angiotensin-aldosterone system (RAAS) plays the main role in the development of this factor, namely, the high activity of angiotensin II (AT II). This hormone has a significant effect on the process of intrarenal hemodynamic disturbances and on the development of structural changes in kidney tissue in diabetes [19,22,24].

**Anemia** is one of the main manifestations of a decrease in kidney function in DN and, at the same time, a factor in the progression of kidney pathology. Thus, anemia in patients with DM1 with DN was detected 2.5 times more often than without kidney damage (41.9% and 16.6%, respectively), and in DM2 - 2.1 times more often (25.7% and 12.0%, respectively) [16,25]. An assessment of the





prevalence of anemia in patients with DN, depending on the stage of CKD and the severity of kidney damage, revealed that the frequency of anemia proportionally increases with increasing albuminuria and decreasing GFR, reaching 89.5% at the pre-dialysis stage of CKD.

The leading link in the pathogenesis of anemia in patients with DN is inadequate production of the hormone erythropoietin (EPO) by the kidneys in response to anemia (hypoxia) - the level of EPO in the blood remains within normal values, i.e. does not correspond to a low Hb value. This phenomenon is called functional or relative EPO deficiency. It has been established that in progressive kidney diseases, the production of EPO kidneys in response to anemia can be maintained at a GFR level of more than 40 ml / min / 1.73 m<sup>2</sup>.

**Conclusions.** Thus, DN is an important problem of modern medicine and the pathogenesis of development has its own characteristics. This problem has not lost its relevance at the present time. Early diagnosis of DN and elimination of risk factors remain the basis in the clinic of internal diseases. The treatment of already the last stage of DN is not only a complex process, but also, due to some economic aspects, very costly. It is easier to engage in the prevention of vascular complications and try to prevent the transition of the disease to the end stage of renal failure than to treat patients with CRF by hemodialysis.

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