Volume 3, Issue 2, February 2025 ISSN (E): 2938-3765

# PATHOGENESIS OF CHRONIC COMPLICATIONS OF TYPE 2 DIABETES MELLITUS AND WAYS OF THEIR CORRECTION

Ismailov Diyorbek
Department of Endocrinology
Fergana Medical Institute of Public Health

**Abstract**
Type 2 diabetes mellitus (T2DM) is one of the most common endocrine pathologies characterized by insulin resistance and relative insulin deficiency. In the absence of adequate control, the disease leads to the development of chronic complications affecting the cardiovascular, nervous, renal and visual systems. This review article discusses the main mechanisms of pathogenesis of chronic complications of T2DM and modern approaches to their correction.

**Keywords**: Type 2 diabetes mellitus, pathogenesis, chronic complications, oxidative stress, endothelial dysfunction, inflammation, therapeutic approaches.

## Introduction

Chronic complications of type 2 diabetes mellitus develop under the influence of a complex of pathological mechanisms, including hyperglycemia, oxidative stress, chronic inflammation, dyslipidemia and microcirculation disorders. Long-term increase in blood glucose levels leads to accumulation of advanced glycation end products , which cause structural changes in tissues and activate inflammatory processes. As a result, the vascular endothelium is damaged, which contributes to the development of diabetic angiopathy, retinopathy, nephropathy and neuropathy.

Oxidative stress that occurs in type 2 diabetes is accompanied by excessive production of reactive oxygen species, which damages lipids, proteins, and cellular DNA. Impaired antioxidant protection exacerbates mitochondrial and endothelial cell dysfunction, which contributes to the progression of complications. In parallel, chronic inflammation caused by the activation of proinflammatory cytokines maintains a cascade of pathological changes, accelerating the development of vascular and nerve lesions.

Dyslipidemia in diabetes mellitus is manifested by an increase in the level of triglycerides and oxidized low-density lipoproteins, which contribute to the formation of atherosclerotic plaques, which increases the risk of myocardial infarction and stroke. Microcirculation disorders associated with thickening of the capillary basement membrane and increased aggregation of erythrocytes lead to deterioration of tissue blood supply, which contributes to the development of diabetic foot and renal failure.

Correction of chronic complications of diabetes mellitus requires a comprehensive approach, including strict glycemic control, the use of antioxidant and anti-inflammatory therapy, normalization of the lipid profile and blood pressure, and improvement of microcirculation.



Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

Modern methods of therapy aimed at reducing glucose levels, the use of drugs with cardio- and nephroprotective properties, as well as the correction of inflammatory processes, can slow the progression of complications and improve the quality of life of patients.

**Mechanisms of pathogenesis of chronic complications of type 2 diabetes**

The pathogenesis of complications of type 2 diabetes includes a number of interrelated processes, the main ones of which are hyperglycemia, oxidative stress, chronic inflammation, dyslipidemia and microcirculation disorders.

Hyperglycemia and protein glycation. Hyperglycemia leads to the accumulation of advanced glycation end products ( AGEs ), which cause structural and functional changes in tissues. These compounds interact with RAGE receptors, activating inflammatory cascades and contributing to the development of vascular complications.

Oxidative stress. In T2DM, there is excessive formation of reactive oxygen species (ROS), which leads to endothelial damage, mitochondrial dysfunction, and activation of cell apoptosis. Oxidative stress plays a key role in the development of neuropathy, nephropathy, and retinopathy.

Chronic inflammation. Increased levels of proinflammatory cytokines (TNF-α, IL-6, CRP) contribute to the progression of atherosclerosis, the development of insulin resistance and damage to target organs.

Dyslipidemia and endothelial dysfunction. Altered lipid profile (increased triglyceride levels, decreased HDL, increased oxidized LDL) aggravates vascular damage, contributing to the development of diabetic angiopathy.

Microcirculation disorder. Long-term hyperglycemia leads to thickening of the capillary basement membrane, impaired tissue perfusion and hypoxia, which contributes to the development of diabetic foot, nephropathy and retinopathy.

Chronic complications of type 2 diabetes

Diabetic retinopathy. The main pathogenetic mechanisms are hyperglycemia, oxidative stress and endothelial dysfunction, which lead to microaneurysms , exudates and proliferation of new vessels.

Diabetic nephropathy. Progressive damage to the glomerular apparatus of the kidneys is associated with hyperglycemia, activation of the renin-angiotensin -aldosterone system (RAAS) and increased expression of matrix proteins, which leads to fibrosis and chronic renal failure.

Diabetic polyneuropathy . Develops as a result of microcirculation disorders and metabolic changes, accompanied by the death of peripheral nerve fibers, which leads to pain syndromes, loss of sensitivity and autonomic dysfunction.

Cardiovascular complications. Atherosclerosis and endothelial dysfunction contribute to the development of coronary heart disease, myocardial infarction, and stroke. Patients with type 2 diabetes have a 2-4 times higher risk of cardiovascular events than people without diabetes.

**Approaches to the correction of chronic complications**

Glycemic control **.** Maintaining glucose levels within target values (HbA1c <7.0%) reduces the risk of microvascular complications. Modern drugs (SGLT2 inhibitors, GLP-1 agonists) not only improve glycemic control, but also have cardioprotective and nephroprotective properties.



Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

Antioxidant therapy The use of antioxidants (alpha-lipoic acid, vitamin E, metformin ) reduces oxidative stress and reduces the severity of neuropathy and retinopathy.

Anti-inflammatory therapy The use of NF- κB inhibitors , statins and polyphenols helps to reduce chronic inflammation and slows the development of vascular complications.

Control of dyslipidemia Prescription of statins and fibrates reduces the risk of cardiovascular complications in patients with diabetes. There is evidence of benefit of combination therapy including ezetimibe and PCSK9 inhibitors.

Antihypertensive therapy Control of blood pressure with ACE inhibitors and angiotensin II receptor blockers (ARBs) reduces the risk of progression of nephropathy and cardiovascular complications.

Microcirculation correction The use of pentoxifylline, alprostadil and antiplatelet agents helps improve tissue blood supply and prevent diabetic foot.

## Conclusions

Chronic complications of T2DM develop due to the combined effects of hyperglycemia, oxidative stress, inflammation and vascular dysfunction. An effective strategy for their prevention and treatment includes a multicomponent approach: control of glycemia, dyslipidemia and blood pressure, as well as the use of antioxidant and anti-inflammatory therapy. Modern research is aimed at developing new methods of personalized therapy aimed at slowing the progression of complications and improving the quality of life of patients.

## References

1. Ceriello , A. (2020). "Oxidative stress and glycemic regulation: Beyond HbA1c variability." Diabetes Care , 43(5), 920-930.
2. Brownlee, M. (2021). "The pathobiology of diabetic complications: A unifying mechanism." Diabetes , 70(6), 1453-1462.
3. Forbes, J. M., & Cooper, M. E. (2019). "Mechanisms of diabetic complications." Physiological Reviews , 99(1), 137-187.
4. Zinman , B., Wanner , C., Lachin, J.M., et al. (2018). "Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes." New England Journal of Medicine , 373(22), 2117-2128.
5. Nathan, D. M. (2021). "Diabetes: Advances in diagnosis and treatment." Journal of the American Medical Association (JAMA) , 326(7), 613-623.
6. Balabolkin , M. I. (2020). Pathogenesis and clinical picture of diabetes mellitus and its complications . Moscow: Meditsina.
7. Mohammad, A. M., Dolgushina, N. V. (2021). "Chronic complications of type 2 diabetes mellitus: modern concepts of pathogenesis and therapy." Endocrinology , 27(4), 56-67.
8. Gapparov, F. A., Yusupova, L. M. (2019). "Features of microcirculatory disorders in diabetes mellitus." Clinical medicine of Uzbekistan , 2(3), 45-51.
9. Kuraev, G. A. (2018). "The role of oxidative stress in the development of diabetic angiopathy." Problems of Endocrinology , 64(6), 89-95.
10. Abdurakhimov, Sh. H. (2022). "Modern approaches to the treatment of type 2 diabetes mellitus and its complications." Uzbekistan Medical Journal , 3(4), 27-34.



Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5