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MORPHOLOGICAL ASPECTS OF DIABETES MELLITUS AND ITS CONSEQUENCES AT THE TISSUE AND CELLULAR LEVELS

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Annotation: This article provides a comprehensive analysis of tissue- and cellular-level alterations observed in the development of type I and type II diabetes mellitus (DM), along with their pathomorphological basis and underlying mechanisms. Morphological damage resulting from microcirculatory disorders, glucotoxicity, lipotoxicity, oxidative stress, mitochondrial dysfunction, and apoptosis is described based on scientific literature. Typical diabetic alterations in various organs — including the kidneys, liver, heart, blood vessels, nervous tissue, and retina — are thoroughly examined. Histological, histochemical, and immunohistochemical research methods were used to analyze existing data, and key markers important for evaluating structural consequences of diabetes are presented. The article aims to deepen understanding of the cellular and molecular mechanisms of diabetes and to morphologically explain the pathogenesis of its clinical complications.

Introduction

Diabetes mellitus, one of the most prevalent metabolic disorders, results from impaired insulin secretion or diminished insulin action, leading to disturbances in carbohydrate, lipid, and protein metabolism. The major danger of diabetes lies not only in persistent hyperglycemia but also in the complex structural and functional abnormalities that develop in nearly all tissues of the body.

Chronic hyperglycemia promotes the accumulation of glycated molecules, metabolic stress, endothelial injury, and sustained oxidative stress. As a result, profound morphological changes arise in the retina, renal glomeruli, myocardial tissue, peripheral nerves, hepatic parenchyma, and vascular structures.

Studying diabetic complications at the tissue level is of major scientific and clinical importance for the prevention of complications, determination of therapeutic strategies, identification of biochemical markers, and development of regenerative treatment approaches.

Main Part

Diabetes mellitus is a multifaceted metabolic disorder affecting all body systems, and its most significant consequences include profound morphological changes at both tissue and cellular levels. Prolonged hyperglycemia plays a central role in its pathogenesis. Elevated glucose activates aberrant intracellular metabolic pathways, disrupts membrane structures and cytoplasmic organelles—especially mitochondria—and ultimately leads to irreversible tissue remodeling. Initially subtle micromorphological injuries eventually progress to macroscopic structural damage manifested as clinical complications.

One of the key pathogenic mechanisms involves non-enzymatic glycation of proteins. Excessive glucose reacts with proteins to form transient Schiff bases and irreversible ketoamines, eventually producing Advanced Glycation End-products (AGEs). These slowly degradable compounds accumulate in tissues for years, resulting in: thickening of collagen fibers; loss of tissue elasticity; increased stiffness of basement membranes; fragility of vascular walls ; accelerated fibrotic processes.

These changes form the structural basis of diabetic angiopathy.

Excess glucose is metabolized via aldose reductase into sorbitol, leading to: increased intracellular osmotic pressure; cellular swelling; membrane destabilization; ion transport disturbances. The retina, renal tubular epithelium, and peripheral nerves are particularly

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susceptible, forming the morphological basis of diabetic retinopathy and neuropathy. Mitochondrial electron transport chain dysfunction results in excessive reactive oxygen species (ROS). ROS cause: DNA strand damage; lipid peroxidation of membranesprotein denaturation; mitochondrial swelling and cristae disruption; dilation of the endoplasmic reticulum.
These alterations promote apoptosis. In diabetes, the Bax/Bcl-2 ratio shifts in favor of apoptosis, caspase cascades are activated, and apoptotic foci appear.
Endothelial cells are highly sensitive to metabolic stress. Hyperglycemia and ROS accumulation lead to: decreased nitric oxide (NO) production; increased endothelin-1 ; vasoconstriction; hypercoagulability and microthrombosis; two-fold thickening of capillary basement membranes; pericyte degeneration; narrowed capillary lumens and impaired microcirculation.Persistent tissue hypoxia develops as a result.

Materials and Methods

To evaluate diabetic morphological changes, the following methods were applied:
1. Analysis of Scientific Literature
Articles from PubMed, Scopus, Elsevier, Springer, and Web of Science (2010–2024) covering molecular, histological, histochemical, and clinical aspects of diabetes were reviewed.
2. Analysis of Morphological Methods
Histological methods: HE staining, PAS reaction, Masson trichrome.
Histochemical methods: Detection of glycogen, collagen, elastin.
Immunohistochemical markers: Oxidative stress: 8-OHdG, iNOS
Fibrosis: TGF-β1, α-SMA, Collagen I/III
Apoptosis: Caspase-3, Bax/Bcl-2 ratio
Endothelial dysfunction: VEGF, eNOS
3. Systemic Analysis of Pathomorphological Processes
Comparative analysis of diabetic nephropathy, retinopathy, neuropathy, cardiomyopathy, and angiopathy, including mitochondrial injury, membrane destabilization, and apoptosis-inducing mechanisms.

Discussion

Morphological changes in diabetes are multifactorial and result from:

- increased ROS and nitrogen radicals
- accumulation of lipid peroxides
- oxidative DNA, protein, and membrane damage
- nuclear pyknosis and karyorrhexis
- cytoplasmic vacuolization
- mitochondrial swelling and cristae rupture
- endoplasmic reticulum dilation

AGE accumulation leads to:

- ✓ thickened collagen fibers
- ✓ stiff vascular walls
- ✓ basement membrane thickening
- ✓ demyelination of peripheral nerves

Microcirculatory failure results in: endothelial injury, impaired blood rheology, vascular fibrosis, persistent tissue hypoxia, necrotic foci,Organ-specific morphological changes.
Kidneys (diabetic nephropathy): basement membrane thickening, mesangial proliferation, Kimmelstiel–Wilson nodules, tubular epithelial degeneration, interstitial fibrosis.
Progresses to chronic renal failure. Retina (diabetic retinopathy):pericyte loss, microaneurysms, retinal microhemorrhages, neovascularization, neuronal degeneration. Heart (diabetic cardiomyopathy): interstitial fibrosis, vacuolization of cardiomyocytes, mitochondrial

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dysfunction, accelerated coronary atherosclerosis. Nervous system (diabetic neuropathy): axonal demyelination, Schwann cell injury, thickened endoneurial capillary membranes, axonal degeneration. Manifested as sensory loss, pain, paresthesia. Liver: fatty degeneration of hepatocytes, pathological glycogen accumulation, mitochondrial damage, portal fibrosis.
Apoptosis and Necrosis Altered Bax/Bcl-2 signaling , Cytochrome-C release, Caspase-3 activation, apoptotic bodies, nuclear homogenization.
Diabetic Angiopathy microangiopathy: capillary thickening, thrombosis, stenosis; macroangiopathy: accelerated atherosclerosis, decreased NO, excess collagen deposition.

Results

The findings demonstrate that diabetes induces complex morphological changes in nearly all organs and tissues. These changes begin at the cellular level—via oxidative stress, glycation, apoptosis, and mitochondrial dysfunction—and progressively lead to fibrosis, necrosis, sclerosis, and degeneration at the organ level. Early detection of morphological markers and detailed assessment of tissue changes are crucial for diagnosing diabetic complications and developing new therapeutic and regenerative strategies.

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