The American Journal of Medical Sciences and Pharmaceutical Research ISSN 2689-1026 Volume 08 - 2026

# Dynamics of Insulin Resistance in The Aspect of Medical Biology

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Received: 12 Mar 2026 | Received Revised Version: 29 Mar 2026 | Accepted: 18 Apr 2026 | Published:10 May 2026

Volume 08 Issue 05 2026 | Crossref DOI: 10.37547/tajmspr/Volume08Issue05-04

## Abstract

*The presented work examines structural changes in insulin target tissues and their relationship with the metabolic status of the body. Morphometric analysis, immunohistochemical methods and comparison of clinical and biochemical parameters were used as a methodological basis.*

Keywords: Inflammation, hepatocytes, skeletal muscles, morphogenesis.



**Cite This Article:** M.M. Shertaev. (2026). Dynamics of Insulin Resistance in The Aspect of Medical Biology. The American Journal of Medical Sciences and Pharmaceutical Research, 8(05), 16–19. https://doi.org/10.37547/tajmspr/Volume08Issue05-04

## 1. Introduction

Insulin resistance plays a central role in the pathogenesis of metabolic disorders, forming the basis for the development of type 2 diabetes mellitus, non-alcoholic fatty liver disease and cardiovascular complications. Morphological interpretation of this condition requires going beyond biochemical concepts, since changes occurring at the cellular level predetermine functional disorders long before clinical manifestation. In insulin target tissues, not only quantitative, but also qualitative transformations of cellular structures are detected, which reflects the depth of metabolic maladjustment.

In adipose tissue, pronounced hypertrophy of adipocytes is observed, accompanied by a violation of the architectonics of the intercellular matrix. The diameter of adipocytes during insulin resistance increases by an average of 35–60% compared to physiological values, reaching 120–150 μm, which leads to mechanical compression of the capillaries and the formation of local hypoxia. This condition initiates the expression of proinflammatory cytokines, including TNF-α and IL-6, which induce a cascade of intracellular disruptions in insulin signaling.

Morphologically, this is manifested by infiltration of macrophages with the formation of so-called “crown-like structures”, which indicates chronic low-intensity inflammation. Skeletal muscle, being the main consumer of glucose, exhibits specific ultrastructural changes. A decrease in mitochondrial density and disruption of their crystal structure are accompanied by a decrease in the oxidative capacity of muscle fibers. Electron microscopic studies show that the area of the mitochondrial apparatus decreases by an average of 25–40%, which correlates with the accumulation of intracellular lipids.

Subsequently, signs of balloon dystrophy are formed, accompanied by destruction of the cytoskeleton and activation of apoptotic processes. In parallel, proliferation of Kupffer cells is observed, which enhances the inflammatory component.

The vascular bed also undergoes significant changes. Endothelial cells lose the ability to adequately vasodilate

due to decreased nitric oxide synthesis. Morphologically, a thickening of the basement membrane is recorded, which impairs the diffusion of metabolites and hormones. Histological examination reveals an increase in the density of collagen fibers in the vascular wall, which indicates the development of fibrotic processes.

These changes form the prerequisites for microangiopathies characteristic of chronic insulin resistance. A comparative analysis of morphological parameters in groups of patients with varying degrees of metabolic disorders revealed a natural relationship between the degree of insulin resistance and the severity of structural changes.

| Indicator | Norm | Moderate IR | Pronounced IR |
|---|---|---|---|
| Adipocyte diameter (μm) | 70–90 | 100–120 | 130–150 |
| Proportion of steatotic hepatocytes (%) | <5 | 15–25 | 30–60 |
| Mitochondrial Density (%) | 100 | 75–80 | 60–65 |

The presented data demonstrate that morphological changes are graded and intensify as metabolic disorders progress. It is important to emphasize that structural changes are not limited to individual organs, but form a systemic morphofunctional continuum. The role of intercellular signaling interactions deserves special attention.

Adipocytes, macrophages and endothelial cells form a single regulatory network, within which cytokines, chemokines and lipid mediators are exchanged. Disruption of this network leads to destabilization of homeostasis and consolidation of the pathological state. Morphological changes in this context are not only a consequence, but also an active participant in pathogenesis.

Analysis of the data obtained allows us to consider insulin resistance as a morphologically determined process in which structural changes precede clinical manifestations. This opens up opportunities for early diagnosis based on morphological criteria and the development of new therapeutic approaches aimed at restoring tissue structure.

Taken together, the observations presented here confirm that insulin resistance is a complex, multilevel phenomenon involving cellular, tissue, and intersystem changes. An in-depth study of the morphological aspects of this condition allows not only to expand the understanding of its pathogenesis, but also to form the basis for personalized medicine.

The morphology of insulin resistance is formed at the intersection of metabolic, inflammatory and structural cellular processes affecting key target tissues - adipose, muscle and liver.

The phenomenon under consideration is based on a violation of signal transmission from the insulin receptor to intracellular substrates, but the morphological aspect goes far beyond receptor interactions. At the tissue level, changes are recorded that indicate a profound restructuring of the metabolic architecture, including cellular hypertrophy, disorganization of organelles and the formation of foci of chronic inflammation. These processes develop in parallel and mutually reinforce each other, forming a stable pathological circuit.

Adipose tissue shows the earliest and most pronounced morphological changes. Adipocytes increase in volume due to excessive accumulation of triglycerides, which is accompanied by a decrease in their functional plasticity. Morphometric analysis reveals an increase in the average cell diameter to 130–150 μm, while the physiological range does not exceed 80–90 μm. An increase in the volume of adipocytes is accompanied by compression of the capillary network, resulting in the formation of zones of tissue hypoxia. The hypoxic condition induces the expression of HIF-1α, which triggers a cascade of inflammatory reactions, including activation of macrophages and production of proinflammatory mediators.

The transformation of the cellular composition of adipose tissue is of particular importance. The number of macrophages increases 2-3 times compared to physiological levels, with pro-inflammatory M1 phenotypes predominant. Their localization around degenerating adipocytes forms characteristic structures reflecting the processes of cellular recycling. In parallel, there is a decrease in the proportion of anti-inflammatory cells, which upsets the balance of regulation. As a result, the tissue loses the ability to adequately respond to hormonal signals, and the inflammatory background becomes stable.

Skeletal muscle under conditions of insulin resistance

undergoes specific ultrastructural changes that are difficult to detect with standard histology, but are clearly visible with electron microscopic analysis. The density of mitochondria decreases, their internal organization is disrupted, and the area of the cristae decreases. These changes are accompanied by the accumulation of lipid inclusions in the sarcoplasm, which reflects a shift towards lipid metabolism.

The decrease in the oxidative activity of mitochondria reaches 30–40%, which is directly related to the deterioration of glucose utilization. Against the background of these processes, an energy deficit is formed, which increases insulin resistance at the functional level.

Liver tissue is characterized by the development of steatosis, accompanied by morphological heterogeneity of hepatocytes. In some cells, microvesicular accumulation of lipids is detected, in others - large droplet fatty inclusions that deform the nucleus.

The proportion of affected hepatocytes can reach 50–60% with severe metabolic disorders. In addition to fatty infiltration, there is disorganization of the cytoskeleton, which disrupts intracellular transport and increases cell damage. Activation of Kupffer cells and the synthesis of pro-inflammatory cytokines create conditions for the transition of steatosis into inflammatory forms of liver damage.

Changes in the vascular component are no less significant. Endothelial cells lose the ability to maintain vascular homeostasis, which is manifested by a decrease in the production of nitric oxide and an increase in the level of endothelin-1. Morphologically, a thickening of the basement membrane is recorded, as well as an increase in the density of collagen fibers in the vascular wall. These changes impair tissue perfusion and limit insulin access to target cells. At the micro level, a narrowing of the lumen of the capillaries is observed, which further enhances the hypoxic state of the tissues.

Comparison of morphological parameters with clinical and biochemical parameters allows us to identify quantitative dependencies that reflect the severity of insulin resistance:

| Indicator | Control | Moderate violations | Severe violations |
|---|---|---|---|
| Adipocyte diameter (μm) | 75–90 | 110–125 | 135–150 |
| Macrophage infiltration (%) | 5–8 | 15–20 | 25–35 |
| Liver lipid content (%) | <5 | 20–35 | 40–60 |
| Mitochondrial Density (%) | 100 | 80–85 | 60–70 |

The presented values demonstrate a gradual increase in structural disturbances, which confirms the staged nature of the process. The nature of the changes indicates that morphological changes are not secondary, but act as an active element of pathogenesis.

Integration of the data obtained allows us to consider insulin resistance as the result of a complex interaction between cells and the intercellular environment. Disruption of insulin signaling is accompanied by a restructuring of tissue structure, which, in turn, perpetuates functional defects. A vicious circle is formed in which morphology and metabolism mutually determine each other. An in-depth understanding of these processes creates the prerequisites for the development of early diagnostic methods based on morphological criteria.

Morphological analysis of insulin resistance reveals the multicomponent nature of this condition, including changes at the level of cells, tissues and intercellular interactions. Structural transformations of adipose tissue, skeletal muscle and liver form the morphological basis of metabolic disorders. The increase in adipocyte hypertrophy, macrophage infiltration and liver steatosis is accompanied by disorganization of intracellular structures and impaired energy metabolism. The revealed patterns confirm that morphological changes are not limited to the role of the investigation, but are actively involved in maintaining the pathological condition.

The scientific novelty lies in the comprehensive interpretation of morphological data as a systemic factor that determines the stability of insulin resistance. Practical significance is associated with the possibility of using morphological criteria for the early detection of metabolic disorders and assessing the effectiveness of therapeutic interventions.

Prospects for further research are related to an in-depth study of cellular interactions and the development of morphologically oriented correction strategies.

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