MORPHO-FUNCTIONAL CHANGES IN THE ENDOCRINE PANCREAS OF WHITE RATS UNDER METABOLIC SYNDROME CONDITIONS

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Abstract. *To assess the morphological characteristics of the pancreas in experimental metabolic syndrome. Materials and Methods: White laboratory rats under hypokinetic conditions were used in the experiment. To achieve the research goal, the pancreases of 51 sexually mature white laboratory rats were examined. The animals were divided into two groups. The first group consisted of intact adult rats (control). In the second group, the rats were placed in a special cage with an area of 150 cm² to induce an experimental metabolic syndrome model. Results: In experimental metabolic syndrome, vacuolization of the cytoplasm, irregular nuclear shape, and nucleolar segmentation were observed in the β-cells of the endocrine part of the pancreas. These changes may be associated with impaired intracellular transport and reduced secretory activity. In α-cells located at the periphery of the islets, increased glucagon expression, chromatin condensation, and indistinct cell boundaries were detected, indicating a disruption of hormonal balance. Conclusion: Under metabolic syndrome conditions, a decrease in the number and size of pancreatic islets, structural abnormalities in β-cells, and mild edema and vascular changes in the surrounding connective tissue were observed. These changes were accompanied by reduced hormonal activity of the gland.*

Keywords: *metabolic syndrome, pancreas, endocrine cells, pancreatic lobule, insulin, glucagon.*

Introduction. In recent years, it has been reported that nearly 60% of the global population has insufficient physical activity to maintain a healthy lifestyle [1]. According to literature sources, physical inactivity is responsible for the deaths of approximately 1.9 million people [5]. Reduced physical activity leads to disruptions in the body's overall metabolism [7]. Over time, changes begin to occur in the cardiovascular, respiratory, musculoskeletal, and endocrine systems [9]. Many sources highlight that hypodynamia is one of the leading causes of metabolic syndrome [15]. Metabolic syndrome leads to multiple metabolic disturbances, increasing the risk of cardiovascular diseases and diabetes mellitus. The pathogenesis of metabolic syndrome involves complex mechanisms and remains a subject with many unresolved issues [2, 6, 11, 14, 18].

Metabolic syndrome (MS) is a complex pathological condition characterized by disturbances in carbohydrate, fat, and protein metabolism, insulin resistance, abdominal obesity, hypertension, and dyslipidemia. It is considered one of the most pressing issues in modern medicine. In recent years, the prevalence of MS has increased significantly. According to the World Health Organization, signs of metabolic syndrome are observed in approximately one-third of adults globally. In the United States, this rate reaches around 35%, while in European countries it ranges between 25–30%. In Uzbekistan, some studies have reported that metabolic syndrome is present in 20–25% of the population [3, 8, 10, 13, 20].

One of the most important factors in the development of metabolic syndrome is hormonal imbalance, particularly the morpho-functional changes occurring in the endocrine part of the pancreas—the islets of Langerhans. Dysfunction of β-cells results in decreased insulin secretion, while overproduction of glucagon by α-cells disrupts glucose metabolism. This leads to hyperglycemia, cellular stress, and inflammatory processes in the body [4, 12, 16, 17, 19, 21].

Today, under conditions of metabolic syndrome, not only hormonal changes but also morphological and histological alterations in the pancreatic islet apparatus, as well as the condition of β- and α-cells, have become a critical focus of research. Understanding the morpho-structural and functional changes in these cells can help in early diagnosis, prevention, and treatment strategies for MS.

Therefore, studying the morphological and functional changes in the endocrine part of the pancreas in an experimental model of metabolic syndrome holds significant scientific and practical value.

Purpose of the Research. Evaluation of the Morphological Characteristics of the Pancreas in Experimental Metabolic Syndrome.

Materials and Methods. The study focused on evaluating the morpho-functional changes occurring in the endocrine part of the pancreas under conditions of metabolic syndrome.

To achieve this goal, 51 sexually mature male white laboratory rats were selected. The rats were divided into two groups: Group 1 — control (intact) rats; Group 2 - experimental group, in which a model of metabolic syndrome was induced over 30 days using a special high-fat diet.

The rats in the experimental group were fed a high-calorie, fat-rich diet, containing up to 65% fat daily. During the experiment, the rats were kept under the same temperature and lighting conditions in the vivarium. Both groups were housed in cages that allowed free movement throughout the experiment.

At the end of the 30-day experiment, the rats were euthanized by decapitation in accordance with the “European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes” (Strasbourg, 1985). Both control and experimental groups were kept in identical vivarium conditions.

For morphometric examination, the NanoZoomer (REF C13140-21.S/N000198/ HAMAMATSU PHOTONICS/431-3196 JAPAN) Hamamatsu system and QuPath-0.4.0 (NanoZoomer Digital Pathology Image) morphometric software were used. The obtained data were statistically processed using the Microsoft Excel 2010 statistical package to calculate the arithmetic mean (M), the standard error (m), and the reliability coefficient (t). Histological images were captured using a CX40 model microscope equipped with an OD400 camera.

Results. In white laboratory rats, the pancreas has an average weight of 208.3 ± 5.8 g and appears pink or pinkish-yellow in color. Anatomically, the pancreas in rats is located in the abdominal cavity, positioned above the lesser curvature of the stomach and along the proximal part of the duodenum. The organ has a trilobed shape, comprising the left lobe - lobus sinister or the gastrosplenic (tail) portion — cauda pancreatis, the middle lobe - lobus medius or the head - caput pancreatis, and the right lobe - lobus dexter.

Our anatomical studies on the rat pancreas revealed three distinct macroscopic parts. The first part - the duodenal portion - is situated within the U-shaped curve of the duodenum, caudal to the opening of the common bile duct. The second part consists of numerous isolated lobules aligned along the bile duct. The third part - the gastrosplenic portion - is located to the left of the first two parts, within the duplication of the gastrosplenic ligament. The main bulk of the pancreas lies adjacent to the stomach, while its lateral region reaches toward the splenic hilum, encasing the main splenic vein through its small penetrating vessels.

In the control group, the organ parenchyma consisted of lobules separated by fine connective tissue, within which blood vessels and ducts were present. The exocrine portion of the pancreas was composed of typical acini. The acini consisted of conical exocrinocytes, which exhibited basophilia at the basal part and acidophilia at the apical portion. The nuclei were round with clearly visible nucleoli. The cytoplasm appeared granular in structure.

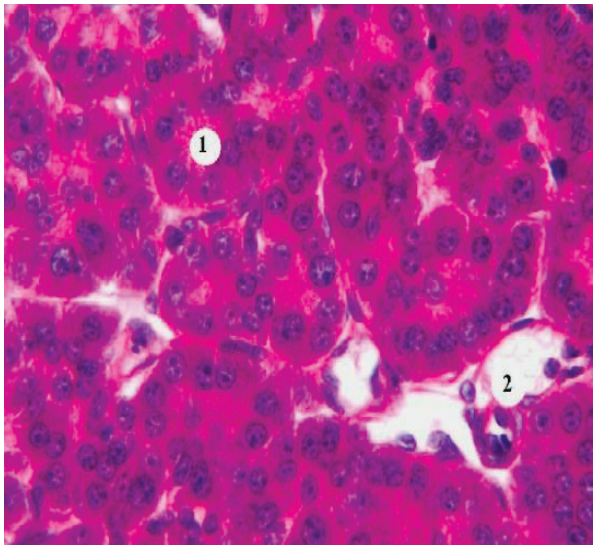

Fig. 1. Histological structure of the pancreas in the control group of rats.
1 – Pancreatic acinar cells, 2 – Blood vessels.
Hematoxylin and eosin staining.
Magnification: 40x10.

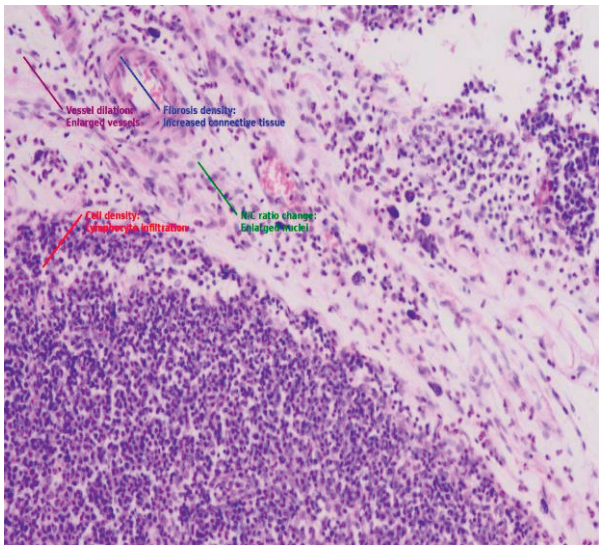

Fig. 2. Histological structure of the pancreas in the experimental group of rats.
Islet structure disruption (blue) – Disorganization of normal architecture and uneven distribution of cells.
Increased fibrosis (green) – Proliferation of connective tissue around the islets.
Lymphocytic infiltration (red) – Development of an inflammatory process.
Vascular dilation (purple) – Impaired microcirculation and ischemic changes.
Hematoxylin and eosin staining.
Magnification: 20x10.

In the experimental group (metabolic syndrome model), significant morphological changes were observed in the pancreas. The shape and arrangement of exocrine acini appeared irregular, with cytoplasmic vacuolization in exocrinocytes, nuclear deformation, and, in some cases, nuclear segmentation. Basal basophilia was reduced, while apical acidophilia was weakened. Most acini were surrounded by slightly edematous connective tissue. The number of endocrine islets was reduced, and their size decreased as well. In β-cells, vacuolization and chromatin condensation were detected. In

α-cells, enhanced glucagon expression was accompanied by nuclear shape irregularities and indistinct cell contours.

Furthermore, the architecture of the pancreatic tissue was significantly disrupted under metabolic syndrome conditions. The borders between lobules became indistinct, and in some areas, an expansion and densification of connective tissue were observed. Dilation of interlobular excretory ducts and blood-filled vessels surrounding them indicated microcirculatory disorders characteristic of metabolic syndrome.

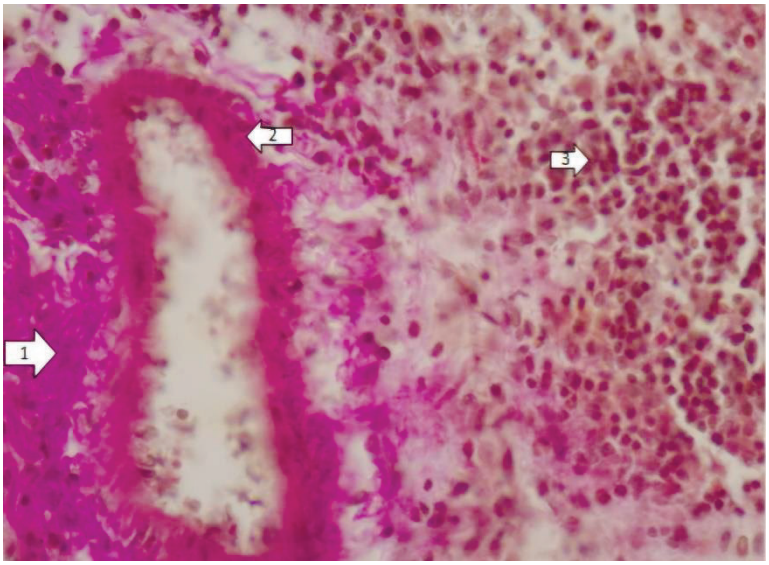

Fig. 3. Histological structure of the pancreas in the experimental group of rats.
Degenerative changes were observed in the pancreatic tissue stained using the Weigert method.Fragmentation of elastic fibers and structural disorganization (1).
Increased cellular infiltration in the connective tissue (2).
Under the influence of metabolic syndrome, increased cellular density and structural changes in the pancreatic parenchyma (3).
Image stained with Weigert method, magnification: 40×10.

Mild edema was observed between the acini, indicating the accumulation of interstitial fluid and disruption of the secretory process. Dilated intralobular ducts were lined with cuboidal or flattened epithelium, and secretory cells were detected in their stroma. These findings suggest pathological alterations in exocrine activity.

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In the endocrine regions, β-cells displayed nuclear shrinkage and signs of karyopyknosis, indicating reduced cellular activity. The area of α-cells decreased by 8.5% compared to the control group, with enlarged nuclei, increased vacuole number, and reduced electron density. Although the total area of secretory granules in α-cells increased, their diameter decreased from 22.7 ± 0.9 nm to 18.4 ± 0.5 nm, reflecting a diminished capacity for hormone production.

According to morphometric measurements, the average diameter of pancreatic acini was 11.4 ± 0.3 μm, and their height was 2.15 ± 0.18 μm. In the experimental group, the diameter decreased by up to 3%, and height by up to 12%. These changes suggest a regressive state of the exocrine component of the pancreas under metabolic syndrome conditions.

Conclusion. The results of the 30-day experimental study demonstrated significant morpho-functional alterations in the pancreas of white laboratory rats under metabolic syndrome conditions. Notably, there was expansion of interlobular connective tissue within the stroma, edema and inflammatory infiltrates in blood vessels, and morphological changes in the excretory ducts. In the exocrine portion, a reduction in the diameter and height of acinar cells, decreased secretory activity, and a decline in morphometric parameters were observed, indicating impaired digestive function of the pancreas.

In the endocrine portion, structural changes in the islets of Langerhans were detected, particularly karyopyknosis and nuclear shrinkage in β-cells, and nuclear deformation along with altered morphometric parameters of secretory granules in α-cells. These findings indicate dysregulation in insulin and glucagon secretion.

Overall, the morpho-functional changes occurring in the exocrine and endocrine components of the pancreas under metabolic syndrome provide a significant experimental foundation for understanding the pathogenesis and complications of this condition.

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