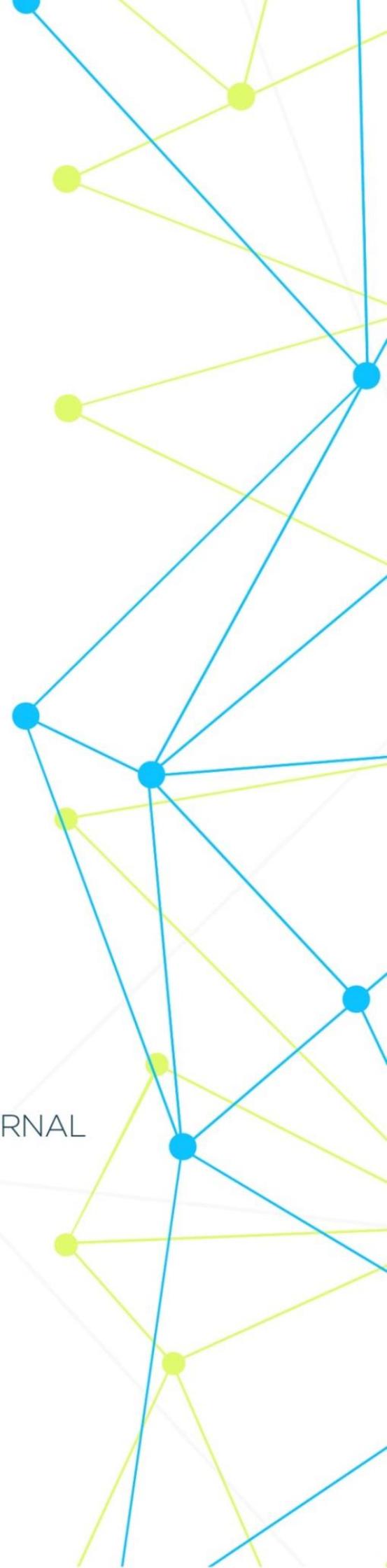


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**Morphological characteristic changes of the kidney tissue of offspring of rats born on the background of diabetes mellitus with streptocyzine**

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**Abstract:** Very complex metabolic disorders are observed in offspring rats born with diabetes. The characteristic features of these disorders are that they affect the organs of the digestive system and end with most dystrophic necrotic and sclerotic changes. In this study, the morphological changes of the kidneys of offspring rats born from mothers with streptothiazine diabetes were studied in the period from 3 to 10 days. During our study, it was found that atrophic and sclerotic changes developed in the kidney balls.

**Keywords:** morphology, kidney, ball, atrophy, sclerosis, diabetes mellitus with streptothiazine.

**Relevance of the subject:** Diabetes mellitus (DM) is a pathological process that continues with insulin deficiency and increased blood glucose due to alteration and necrosis of beta cells in the islets of Langerhans. The total number of people suffering from diabetes in the world is 38.8%, and type 1 diabetes occurs mainly in young children and adolescents aged 5-14 years. Including, in the period after the current post-covid pandemic, the incidence of type 1 diabetes mellitus, which was first detected in adolescents, is increasing. Such problems make our research urgent. The presence of streptothiazine in the composition of drugs used for polychemotherapy used in the treatment of malignant neoplasms during pregnancy continues with the development of specific morphological changes in the internal organs of the offspring, including the kidney tissue. A criterion that allows predicting the changes that may lead to the development of kidney pathologies observed in babies born to these mothers has not been fully developed. In our research work, the periodicity of the changes and development of the kidneys of offspring rats born on the background of streptothiazine diabetes in their mother was studied, and the results obtained through specific morphological and morphometric changes were analyzed and recommendations were made that would allow for prospective forecasting.

Hyperglycemia during pregnancy disrupts the intrauterine environment, affects the normal development of the fetus, and has long-term effects on the function and structure of the fetal pancreatic islets [1]. This condition increases the risk of obesity/obesity, glucose intolerance and type 2 diabetes later in life [2]. Animal studies have shown that the offspring of diabetic rats can become insulin resistant and diabetic [3]. Research supports the concept that developing organs have critical periods of intense structural and functional reorganization. In the case of the pancreas, this condition may make it vulnerable to environmental stimuli [4], which may have consequences for the next generation, and future studies should address the interactions between hormones involved in this glucose control [5]. .

**Objective** To study the morphological changes of renal nephrons in the offspring of rats with streptozotocin diabetes.

**Materials and methods:** As an object of research to achieve the goal set before us, as well as to fulfill the tasks 60 Wistar white laboratory rats in the postnatal period were used.

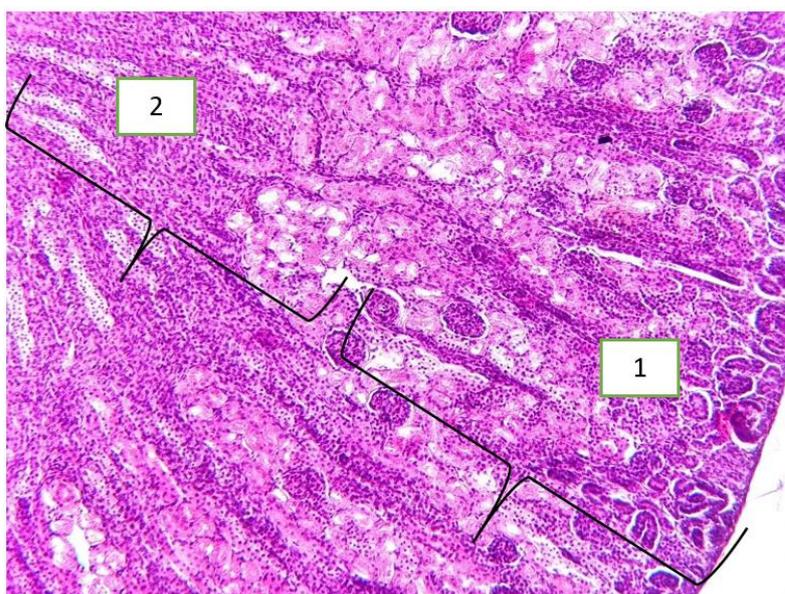
Rats were divided into 2 groups. The first group was the experimental group. In the experimental group, pregnant white laboratory rats were given an experimental model of diabetes by intraperitoneal injection of streptozocin (Streptozocin, Sigma) at a dose of 40 mg/kg in a single injection volume of 0.5 ml in Citrate buffer (Citratebuffer solution, 0.09M, Sigma).

The second group was the control group, in which 0.9% physiological solution was injected into the abdominal cavity of rats. We periodically draw blood from the tail vein from the rats in the control and experimental groups and analyze the blood and urine glucose levels on the automatic biochemical and enzyme immunoassay analyzer ChemWell 2910 Combi.

Rats were euthanized by decapitation at different periods of postnatal ontogeny. We studied ontogenesis in the following periods of postnatal ontogenesis: 3 days, 10 days, 30 days.

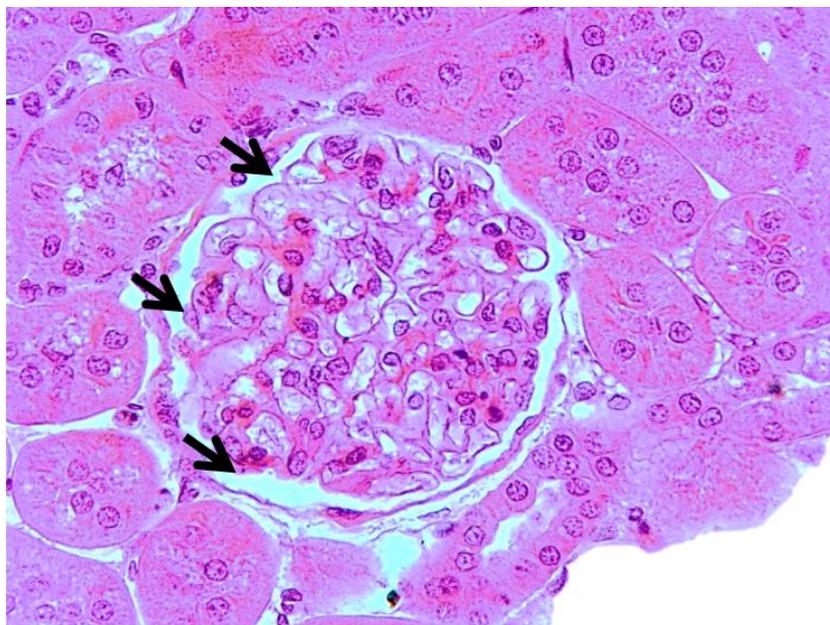
A set of morphological research methods is used in the work: general histological, morphometric research methods.

**Research results and their discussion: Day 3** In experimental conditions, streptozocin solution sent to the abdominal cavity of rats leads to the development of a typical pathological process in the form of blood circulation disorders due to the fact that it increases the amount of sugar in the blood and increases the rheological parameters of the blood. The fact that hyperglycemia induced by this experiment did not induce noticeable changes during the first 3 days is reflected in Figures 1 and 2. On the 3rd day, the kidneys of the rats showed signs of fullness, mainly in the capillaries in the balls. In this case, as a result of strong reabsorption of the epithelium of the proximal tubules, the accumulation of SHIK-positive structures in the cytoplasm is observed.



**Figure 1** . Overview of the histological structure of the kidney. Shows the cortex (1) and medulla (2) of the kidney. Most of the balls have the same round and oval shape. In the medulla, the canaliculi consist of aggregates. Dye Hematoxylin eosin. Size 4x10.

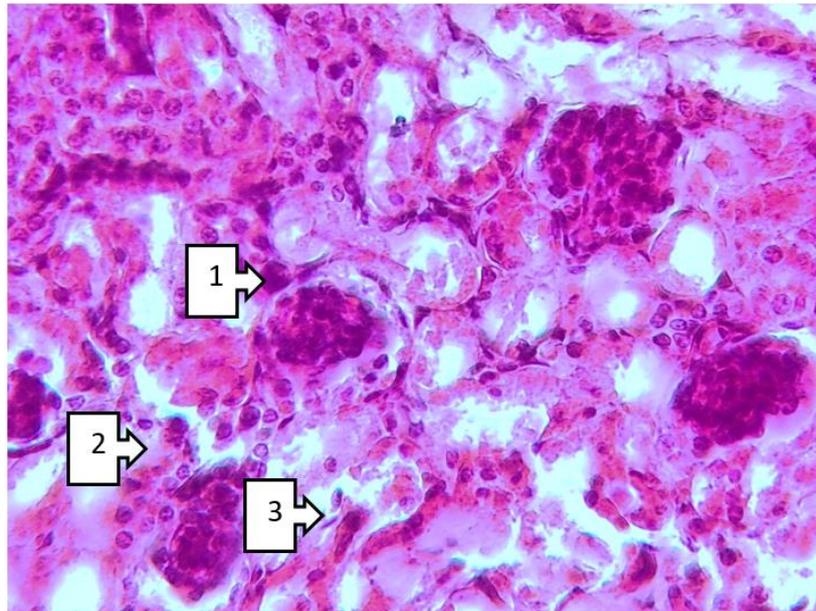
It is accompanied by fullness in paracanalicular vessels and the development of low-level interstitial edema. In our study, on the 3rd day, the blood vessels of the blood vessels were filled, the swelling in Bowman's space was weakly formed, the main changes were the development of hyaline droplets and hydropic dystrophy in the epithelia of the proximal canals. At the same time, the presence of partially mesh-like protein structures was detected in the distal tubules.



**Figure 2.** General view of kidney balls. The structure of the balls is unchanged. Bowman's space is almost the same width (indicated by the arrow). Most of the mesangial cells are found in the cavity of the ball (1), the epithelium of the proximal and distal tubules around them are stained dark and light, no changes are detected. Dye hematoxylin eosin. Size 20x10.

**Day 10.** Morphological changes of kidney nephron system and cortical layer after experimental intraperitoneal delivery of rats.

The periphery of the balls is characterized by the hypertrophy of the proximal tubular epithelia and the increase of basophilic and oxyphilic inclusions in the cytoplasm. In the epithelia of the distal tubules, hyaline droplet dystrophy is detected, in the tubule spaces, reticular homogeneous protein structures are detected. The presence of these mesh-like homogeneous structures in the primary urine filtered in diabetes is caused by insufficient reabsorption of the increased glucose and oxygen components in the tubular epithelia, as a result of the absorption of proteins and carbohydrates into the cytoplasm of many cells in the infiltration mechanism, the enlargement of the tubular epithelia leads to the narrowing of the tubular cavity and the humidification of the fluids in the tubular cavity. These changes, in turn, lead clinically to the excretion of urine glucose and protein and to the diminution per unit time of the primary urine filtered in the glomerular cavity.



**3 - Fig.** Proliferative activity of mesangial cells is clearly depicted in Bowman's space around the balls (1), proliferation of mesangial cells causes deformation in the ball (2), foci of monocellular necrosis are detected in the epithelium of the proximal tubules (3). Paint G-E. 40x10.

This, in turn, leads to an increase in the hydrostatic pressure in the Bowman's space compared to the hydrostatic pressure in the capillaries of the "wonderful mesh", as a result of which the proliferative activity of mesangial cells sharply increases, which leads to the formation of sparse fibrous connective tissue components in the Bowman's space. As these structures begin to appear in the uppermost part of the glomerulus, they accumulate in the form of a cap, resulting in the appearance of "ball cap" diabetic glomerulosclerosis.

**30th day** . Morphological changes in the renal nephron system and cortex after experimental intraperitoneal delivery of rats.

The main pathogenesis of induced diabetes in experimental conditions begins with the pathology of small-caliber blood vessels. Complex pathophysiological processes include protein glycosylation, hormone-induced cytokine release (eg, transforming growth factor-beta), mesangial matrix deposition, and changes in glomerular hemodynamics. Hyperfiltration, early functional pathology is only a relative indicator of the development of kidney failure.

Hyperglycemia leads to glycosylation of glomerular proteins, which can lead to mesangial cell proliferation, matrix expansion, and vascular endothelial injury. The glomerular basement membrane is usually thickened. Diabetic nephropathy begins with glomerular hyperfiltration (increased glomerular filtration rate [GFR]); GFR normalizes with early renal injury and mild hypertension and worsens with time.

Then microalbuminuria develops, the excretion of albumin in the urine ranges from 30 to 300 mg per day. The detection of albumin in the urine at these concentrations is called microalbuminuria, because the detection of proteinuria in routine urinalysis is possible only when the albumin level is > 300 mg/day. From a microscopic point of view, these mentioned processes lead to the formation of protein and carbohydrate homogeneous mesh structures in the spaces of the proximal tubules and distal tubules of the kidney, to the moistening of the urine that has not been

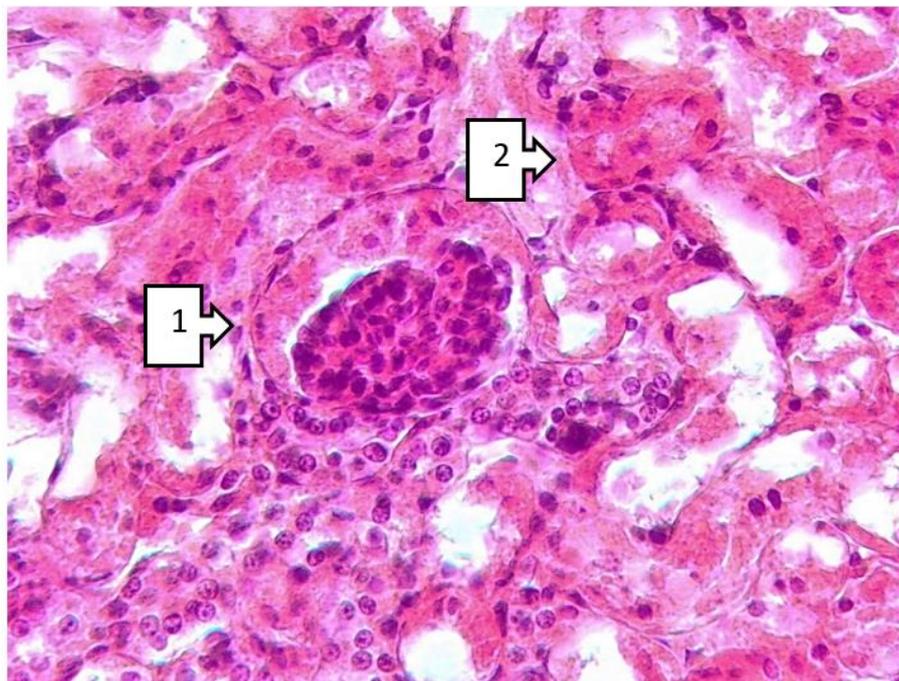
reabsorbed in the spaces of the tubules, and to a slight increase in the hydrostatic pressure in the glomeruli.

As a result, it leads to the sharp formation of hemispherical enlargements. In diabetic nephropathy, the kidneys are usually normal in size or enlarged.

Diffuse or nodular diabetic glomerulosclerosis lesions are characteristic; areas of nodular glomerulosclerosis may appear as Kimmelstiel-Wilson nodules. There is significant hyalinosis and atherosclerosis of afferent and efferent arterioles, interstitial fibrosis and tubular atrophy may be present. Only an increase in mesangial matrix is associated with progression to end-stage renal disease.

In 30 days, the development of the following changes was shown microscopically in the cortex and medulla of the kidneys.

The formation of clear mesangioproliferative foci in most of the seminodal spaces in the balls, the development of hyalinosis and sclerotic changes of the afferent and efferent vessels entering the balls are determined. In particular, it was found that the accumulation of podocytes at the edge of the capillaries in the remarkable network structures, manifested in the form of focal proliferation of mesangial cells (see Fig. 4). But if we take into account that the typical nephropathic glomerulosclerosis manifests itself in the long term, in our work the improving form of this process is determined.



**Figure 4.** Compression compression of the capillaries of the ball, proliferation of mesangial cells of a semicircular shape (1), atrophy and dystrophic changes of the epithelium of the proximal canals around the ball (2). Foci of segmental necrosis are identified in the proximal tubules (3). Paint G-E.40x10.

#### **Kidney tissue morphometry.**

Morphometric indicators of the renal cortical branch, proximal and distal tubular branch of the kidney (table 1-2-3).

**Table 1**

Day 3 white rat kidney corpuscle	Don't worry (M ± m)		
of the capsule parietal of the sheet thickness Shumlyansky - Bowman, mcm		±	
	0.375092	0.075533	0.364167
Shumlyansky-Bowman capsule with glomerulus area, μm <sup>2</sup>	4630,537	720.3992	4495,667
Kidney in his body urine of the cavity area, μm <sup>2</sup>	1343,807	295.3525	1304,667
Glomerular capillary rings area, μm <sup>2</sup>	3323,553	501.2667	3226.75

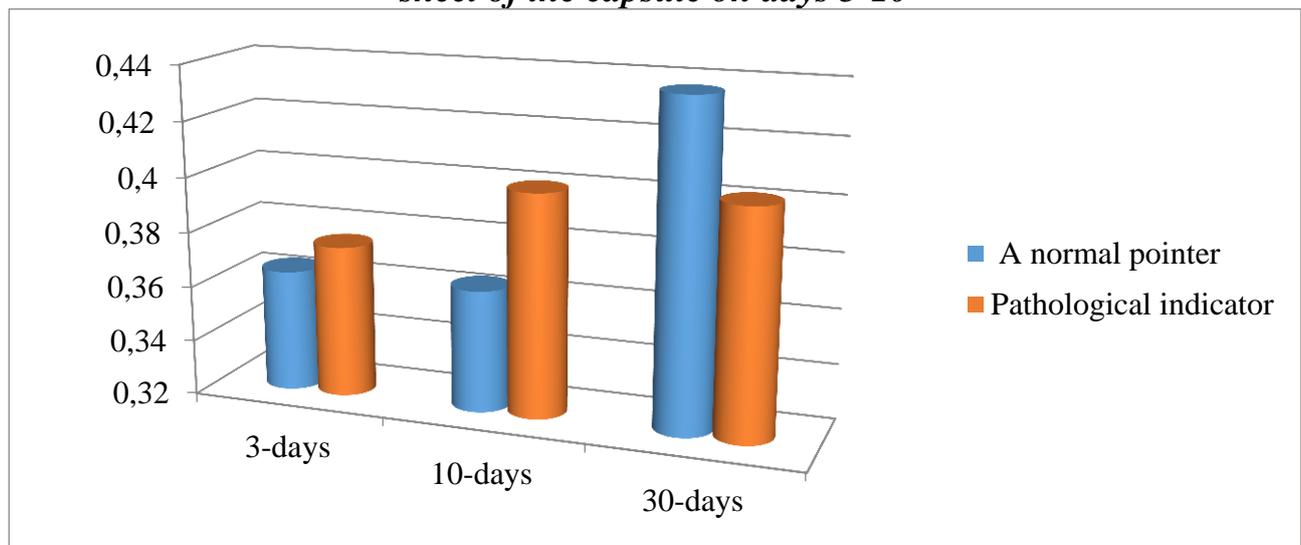
**Table 2**

10-day white calm kidney body	Value (M ± m)		
of the capsule parietal of the sheet thickness Shumlyansky - Bowman, mcm		±	
	0.400583	0.080667	0.364167
Shumlyansky-Bowman capsule with glomerulus area, μm <sup>2</sup>	4945,233	769.3583	4495,667
Kidney in his body urine of the cavity area, μm <sup>2</sup>	1435,133	315,425	1304,667
Glomerular capillary rings area, μm <sup>2</sup>	3549,425	535.3333	3226.75

**Table 2**

30-day white calm kidney body	Value (M ± m)		
of the capsule parietal of the sheet thickness Shumlyansky - Bowman, mcm		±	
	0.40204	0.08096	0.437
Shumlyansky-Bowman capsule with glomerulus area, μm <sup>2</sup>	4963,216	772,156	5394.8
Kidney in his body urine of the cavity area, μm <sup>2</sup>	1440,352	316,572	1565.6
Glomerular capillary rings area, μm <sup>2</sup>	3562,332	537.28	3872.1

**Comparison of normal and pathological indicators of the thickness of the parietal sheet of the capsule on days 3-10**



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