**B.T. Allaberdiev**
**A.B. Akhrorova**

Tashkent State Medical University
Tashkent, Republic of Uzbekistan

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# RELEVANCE OF DIABETES MELLITUS, EPIDEMIOLOGICAL SITUATION, AND CLINICAL-MORPHOLOGICAL FEATURES IN UZBEKISTAN

**Allaberdiev B.T. ✉, Akhrorova A.B. Relevance of Diabetes Mellitus, Epidemiological Situation, and Clinical-Morphological Features in Uzbekistan.**
**Tashkent State Medical University, Tashkent, Republic of Uzbekistan.**

**ABSTRACT. Background.** Diabetes mellitus (DM) is one of the most prevalent chronic endocrine disorders worldwide and is characterized by persistent hyperglycemia and the development of microvascular and macrovascular complications. Despite the increasing global burden of the disease, data on the clinical and morphological characteristics of diabetes in Central Asian countries, including the Republic of Uzbekistan, remain limited. **Objective.** To analyze the clinical and morphological features of diabetes mellitus in patients from the Republic of Uzbekistan and to assess the relationship between histopathological changes and clinical manifestations of the disease. **Methods.** A cross-sectional descriptive study was conducted involving 230 patients with type 1 and type 2 diabetes mellitus observed between 2022 and 2024. Clinical, biochemical, and instrumental parameters were evaluated, including glycemic con-trol, HbA1c levels, renal function, and ophthalmological status. Morphological analysis was performed on tissue samples of the pancreas, kidneys, and retina obtained from autopsy material and ante-mortem renal biopsies. Standard his-tological staining techniques and morphometric analysis were applied. Statistical analysis included comparative and correlation methods. **Results.** Poor glycemic control (HbA1c > 7%) was observed in 92.2% of patients. Morphological examination revealed degeneration of pancreatic β-cells with fibrotic replacement, pronounced glomerulosclerosis, and characteristic features of diabetic retinopathy, including retinal neovascularization. The severity of morphological changes showed a significant correlation with disease duration and HbA1c levels ($p < 0.01$). A substantial proportion of patients demonstrated combined involvement of multiple target organs. **Conclusion.** Diabetes mellitus in the Republic of Uzbekistan is associated with marked clinical and morphological alterations closely related to inadequate glycemic control and longer disease duration. These findings highlight the importance of early diagnosis and optimization of therapeutic strategies to prevent the prog-ression of diabetic complications.

**Key words:** diabetes mellitus, morphology, diabetic nephropathy, diabetic retinopathy, β-cells, microangiopathy.

**Allaberdiev B.T. 0009-0001-4914-9418; Akhrorova A.B. 0000-0002-0937-2316**
**For correspondence: ✉ albotir12@gmail.com**



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## Introduction

Diabetes mellitus (DM) is a chronic metabolic and endocrine disease characterized by persistent hyperglycemia resulting from impaired insulin secretion, decreased tissue sensitivity to its action, or a combination of both. The disease is accompanied by disturbances in carbohydrate, lipid, and protein metabolism and leads to the development of a wide range of micro- and macroangiopathic complications.

According to the World Health Organization (WHO, 2023), more than 540 million people worldwide suffer from various forms of diabetes mellitus [1], and the International Diabetes Federation projects that this number may exceed 700 million by 2045 [2]. The increasing prevalence of the disease is associated with global epidemiological changes and lifestyle factors, including urbanization, obesity, and physical inactivity. In low- and middle-income countries, the burden of DM is particularly high due to late diagnosis, limited coverage of screening programs, and insufficient access to specialized medical care.

In the Republic of Uzbekistan, the epidemiological profile of diabetes mellitus generally reflects global trends [3]. According to the Agency of Statistics under the President of the Republic of Uzbekistan (2024), more than 230,000 patients are officially registered with a diagnosis of diabetes [7]. However, epidemiological models based on population studies indicate that the true prevalence of the disease among the adult population may reach 7.9%, indicating a significant proportion of undiagnosed cases.

The increase in incidence is accompanied by an increase in the frequency of complications, including diabetic nephropathy, retinopathy, neuropathy, and cardiovascular disorders. Morphological examination of tissues in diabetes mellitus allows for a deeper understanding of the pathophysiological mechanisms of the disease. Histopathological examination of the pancreas, kidneys, and retina reveals structural changes that determine disease progression and the development of complications, and comparison of morphological data with clinical indicators helps improve approaches to early diagnosis and therapy.

Given the limited clinical and morphological data from Central Asian countries, including Uzbekistan, this study aims to analyze the clinical and histological features of diabetes mellitus in patients seen between 2022 and 2024.

**Objective**

To analyze the clinical and morphological features of diabetes mellitus in patients from the Republic of Uzbekistan and to identify the relationship between histopathological changes and clinical manifestations of the disease observed between 2022 and 2024.

**Materials and methods**

This study was a descriptive, cross-sectional study conducted from January 2022 to December 2024 at the Central Clinical Hospital of Tashkent (Republic of Uzbekistan). The study aimed to evaluate the clinical, biochemical, and morphological features of patients with a confirmed diagnosis of diabetes mellitus.

The study protocol was reviewed and approved by the Ethics Committee of Tashkent State Medical University (Protocol No. 2021/12-E dated December 15, 2021). All participants provided written informed consent prior to inclusion in the study. The study was conducted in accordance with the principles of the 2013 Declaration of Helsinki for Biomedical Research Involving Human Subjects.

*Study population*

The study included 230 patients (92 men and 138 women) aged 35 to 75 years.

Inclusion criteria:

• Confirmed diagnosis of type 1 or type 2 diabetes mellitus according to the WHO diagnostic criteria (2023):

o Fasting plasma glucose ≥ 7.0 mmol/L, or

o HbA1c ≥ 6.5%, or

o 2-hour post-load plasma glucose ≥ 11.1 mmol/L

• Age 35 to 75 years

• Disease duration of at least 1 year

• Willingness to participate in the study

Exclusion criteria:

• Secondary forms of diabetes (pancreatogenic, drug-induced, endocrinopathies)

• Acute infectious diseases at the time of examination

• Malignant neoplasms

• Pregnancy and lactation

• Refusal to participate in the study

Distribution by diabetes type:

• Type 1 diabetes mellitus: 126 patients (55%)

o Moderate Age: 42.3 ± 11.2 years

o Average disease duration: 14.6 ± 6.8 years

• Type 2 diabetes mellitus: 104 patients (45%)

o Average age: 62.1 ± 8.4 years

o Average disease duration: 9.2 ± 5.3 years

*Note:*

The high proportion of patients with type 1 diabetes in this sample (55%) does not reflect the population distribution of diabetes types and is explained by the specific clinical setting of the study. The Tashkent Central Clinical Hospital is a specialized endocrinology center of national significance, where patients with type 1 diabetes are referred from all over Uzbekistan for insulin therapy and treatment of complications. As is the case worldwide, type 2 diabetes predominates in this population (approximately 90% of all diabetes cases).

All patients underwent a comprehensive clinical and laboratory examination at inclusion.

*Clinical and biochemical assessment*

Clinical data were collected from medical records, physical examination, and laboratory tests.

*Glycemic control assessment:*

• Fasting plasma glucose (venous blood, glucose oxidase method)

• Glycated hemoglobin (HbA1c) – high-performance liquid chromatography (HPLC)

*Renal function assessment:*

• Serum creatinine (kinetic Jaffe method)

• Estimated glomerular filtration rate (eGFR) using the CKD-EPI formula

• Urine microalbuminuria test (immunoturbidimetric method)

• Daily proteinuria

*Ophthalmological examination:*

• Visometry (visual acuity)

• Ophthalmoscopy with drug-induced mydriasis

• Optical coherence tomography (OCT) of the retina (Cirrus HD-OCT, Carl Zeiss Meditec)

• Classification of diabetic retinopathy according to the recommendations of the International Council of Ophthalmology (ICO, 2018)

*Cardiovascular assessment:*

• 12-lead electrocardiography (ECG)

• Blood pressure monitoring

• Assessment of cardiovascular history (myocardial infarction, stroke)

*Histopathological and morphological analysis*

Morphological analysis was performed on pancreatic, kidney, and retinal tissue samples obtained from the following sources:

A. Postmortem material (autopsy): Pancreatic, kidney, and retinal tissue samples were obtained from postmortem examinations of 45 patients from the total cohort (19.6%) who died from complications of diabetes or related diseases between 2022 and 2024. Written consent from the relatives of the deceased was obtained for autopsy and sample collection in accordance with the legislation of the Republic of Uzbekistan. Autopsy was performed within 6-12 hours after death.

B. Vitality kidney biopsy: Renal tissue biopsies were obtained from 18 patients (7.8%) during diagnostic percutaneous kidney biopsy for the following clinical indications:

• Progressive proteinuria (> 1 g/day) of unknown etiology

• Rapid decline in renal function (eGFR decline > 5 mL/min/1.73 m² per year)

• Nephrotic syndrome

• Suspected concomitant glomerulopathy

The procedure was performed under ultrasound guidance using a 16G automated biopsy needle. All patients signed informed consent explaining the risks of the procedure (bleeding, pneumothorax, infection).

*Note:*

Pancreatic biopsy was not performed in vitality patients due to the high risk of complications (pancreatitis, bleeding, pseudocyst formation) and the lack of clinical indications.

*Tissue processing and staining:*

Tissue samples were fixed in 10% neutral buffered formalin (pH 7.2–7.4) for 24–48 hours at room temperature, then washed with running water, dehydrated in increasing concentrations of alcohol (70%, 80%, 96%, 100%), embedded in paraffin blocks, and sectioned on a microtome into 4–5 μm thick sections.

*Staining methods:*

1. Hematoxylin and eosin (H&E) – to assess the overall morphological picture and cellular architecture

2. Periodic acid–Schiff (PAS) reaction – to visualize thickening of the glomerular basement membranes, mesangial matrix, and glycogen

3. Masson trichrome – to assess fibrosis, collagen deposition, and sclerotic changes

Microscopic examination was performed using an Olympus CX43 light microscope (Olympus Corporation, Japan) at magnifications of ×100, ×200, and ×400. Photomicrography was performed using a high-resolution digital camera.

*Morphometric analysis:*

To quantify morphological changes, the following measurements were performed:

• Glomerular basement membrane thickness (average of 10 measurements)

• Mesangial matrix area (ImageJ software)

• Retinal capillary density (number of capillaries per 1 mm² of tissue)

All morphological observations were independently assessed by two experienced pathologists (with over 15 years of experience) to ensure diagnostic accuracy and reproducibility of the results. In case of discrepancies, an additional advisory review of the slides by a third expert was performed. The inter-rater agreement coefficient (Cohen's kappa) was 0.89, which corresponds to an excellent level of agreement.

*Statistical analysis*

Statistical data processing was performed using SPSS version 26.0 (IBM Corp., USA) and GraphPad Prism 9.0.

Descriptive statistics: For normally distributed quantitative variables, data are presented as mean ± standard deviation (M ± SD). For non-normally distributed variables, the median and interquartile range (25th; 75th percentiles) were used. Categorical data are presented as absolute numbers and percentages.

Test of normality: The Shapiro-Wilk test was used to assess the normality of distribution of quantitative variables.

*Comparative analysis:*

• To compare two independent groups (types 1 and 2 diabetes), the Student's t-test was used for normal distributions; for abnormal distributions, the Mann-Whitney U-test was used.

• To compare categorical variables, the Pearson chi-square test or Fisher's exact test (for expected frequencies < 5) were used.

Correlation analysis: To assess the relationship between morphological changes and biochemical parameters (HbA1c, eGFR, disease duration), the Pearson correlation coefficient (for normal distributions) or Spearman's rank correlation coefficient (for abnormal distributions) was used.

Significance level: Differences were considered statistically significant at $p < 0.05$. Bonferroni's correction was used for multiple comparisons.

Sample size calculation: With an expected difference in mean HbA1c values between groups of 1.5%, a standard deviation of 1.1%, a power of 80%, and a significance level of $\alpha = 0.05$, the minimum required sample size is 11 subjects per group. The actual sample size (n = 230) provides sufficient statistical power (>99%) to detect clinically significant differences.

*Methodological Justification*

The methods of histological processing and tissue staining used complied with generally accepted standards of morphological diagnostics described in pathological anatomy guidelines [6]. Pathological assessment of diabetic nephropathy was conducted taking into account current understanding of the pathogenesis and morphological criteria of kidney damage

in diabetes mellitus, as outlined in international clinical reviews [4]. Morphological classification and interpretation of retinal changes were based on the International Council of Ophthalmology recommendations for the diagnosis and staging of diabetic retinopathy [5]. The statistical methods used correspond to standard biomedical research.

**Results**

*3.1. Clinical characteristics of patients*

A total of 230 patients with a confirmed diagnosis of diabetes mellitus (DM) were examined: 92 men (40.0%) and 138 women (60.0%), aged 35 to 75 years. The mean age was 58.0 ± 9.6 years, the mean disease duration was 12.2 ± 6.5 years. Type 1 diabetes was diagnosed in 126 patients (55%), type 2 diabetes — in 104 patients (45%). Patients with type 1 diabetes were significantly younger (42.3 ± 11.2 years) compared with patients with type 2 diabetes (62.1 ± 8.4 years; $p < 0.001$) and had a longer disease duration (14.6 ± 6.8 vs. 9.2 ± 5.3 years; $p < 0.001$). Body mass index was higher in patients with type 2 diabetes (33.5 ± 4.6 kg/m²; $p < 0.001$). The most common clinical manifestations were polyuria (81%), polydipsia (76%), and fatigue (68%). Insufficient glycemic control (HbA1c > 7%) was found in 92.2% of patients [1, 2].

Table 1

Demographic and clinical characteristics of patients

| Indicator | Total (n=230) | Type 1 diabetes (n=126) | Type 2 diabetes (n=104) | p-value |
|---|---|---|---|---|
| Age, years (M ± SD) | 58,0 ± 9,6 | 42,3 ± 11,2 | 62,1 ± 8,4 | < 0,001 |
| Men, n (%) | 92 (40,0) | 54 (42,9) | 38 (36,5) | 0,332 |
| Women, n (%) | 138 (60,0) | 72 (57,1) | 66 (63,5) | 0,332 |
| Duration of diabetes, years (M ± SD) | 12,2 ± 6,5 | 14,6 ± 6,8 | 9,2 ± 5,3 | < 0,001 |
| BMI, kg/m² (M ± SD) | 28,4 ± 5,2 | 24,1 ± 3,8 | 33,5 ± 4,6 | < 0,001 |

*3.2. Biochemical and functional parameters*

The mean fasting glucose level was 10.6 ± 2.4 mmol/L, HbA1c — 8.9 ± 1.1%. Moderate and severe renal function impairment (eGFR < 60 ml/min/1.73 m²) was detected in 39.1% of patients. Microalbuminuria was diagnosed in 48.7%, proteinuria — in 20.9% of those examined [4]. Diabetic retinopathy was detected in 97 patients (42.2%), of which the proliferative form — in 10.0%. Cardiovascular complications were recorded in 42.2% of patients, including arterial hypertension (71.3%) and coronary heart disease (33.9%).

Table 2

Biochemical Parameters

| Indicator | Value (M ± SD) | Range | Norm |
|---|---|---|---|
| Fasting glucose, mmol/L | 10,6 ± 2,4 | 6,8–17,2 | 3,9–6,1 |
| HbA1c, % | 8,9 ± 1,1 | 6,5–11,8 | < 5,7 |
| Creatinine, µmol/L | 156 ± 68 | 62–412 | 62–115 |
| eGFR, mL/min/1.73 m² | 68 ± 28 | 12–118 | > 90 |
| Total cholesterol, mmol/L | 5,8 ± 1,2 | 3,2–9,4 | < 5,2 |

*3.3. Morphological changes in the pancreas*

Histological examination of postmortem pancreatic specimens (n = 45) revealed varying degrees of β-cell degeneration in the islets of Langerhans, a decrease in islet size and number (Fig. 1), and partial or complete fibrous replacement (58% of specimens).

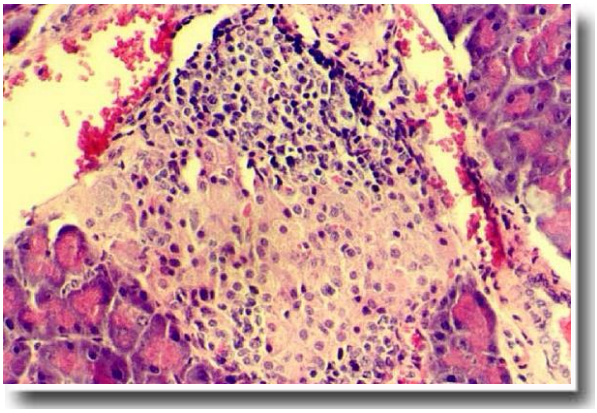

Fig. 1. β-cell degeneration in the islets of Langerhans. Islet architecture is disrupted and partially replaced by fibrous connective tissue. Hematoxylin and eosin staining. ×400.

Patients with type 1 diabetes were more likely to have lymphocytic infiltration of the islets (insulitis). The degree of β-cell degeneration significantly correlated with disease duration ($r = 0.72$; $p < 0.001$) and HbA1c levels ($r = 0.58$; $p < 0.01$).

*3.4. Morphological changes in renal tissue*

Renal tissue revealed typical features of diabetic nephropathy: mesangial dilation, thickening of the glomerular basement membranes, and glomerulosclerosis, including the Kimmelstiel-Wilson nodular type (Fig. 2).

Arteriolar hyalinosis and interstitial fibrosis were present in the majority of cases. The severity of glomerulosclerosis significantly correlated with a decrease in eGFR ($r = −0.81$; $p < 0.001$) and serum creatinine levels ($p < 0.01$).

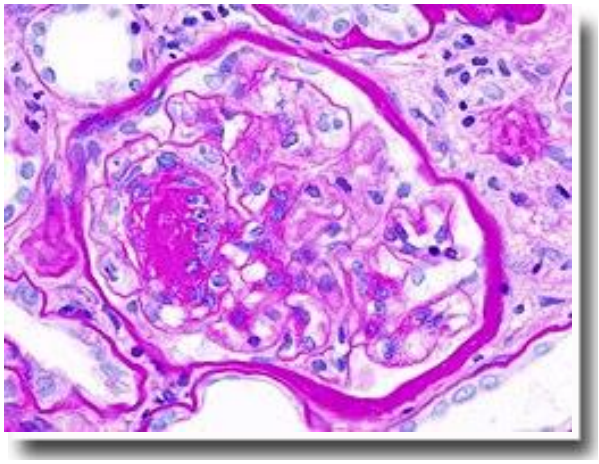

Fig. 2. Diffuse and nodular glomerulosclerosis with thickening of the glomerular capillary loops and Bowman's capsule. Hematoxylin and eosin staining. ×400.

*3.5. Morphological changes in the retina*

Morphological analysis of the retina revealed signs of diabetic retinopathy with a predominance of microangiopathic changes. The main findings were thickening of capillary basement membranes, loss of pericytes (87% of samples), microaneurysms, and areas of ischemia (Fig. 3). Retinal neovascularization was observed in 48% of cases and was associated with diabetes duration ($r = 0.79$; $p < 0.001$) and HbA1c levels ($r = 0.71$; $p < 0.001$).

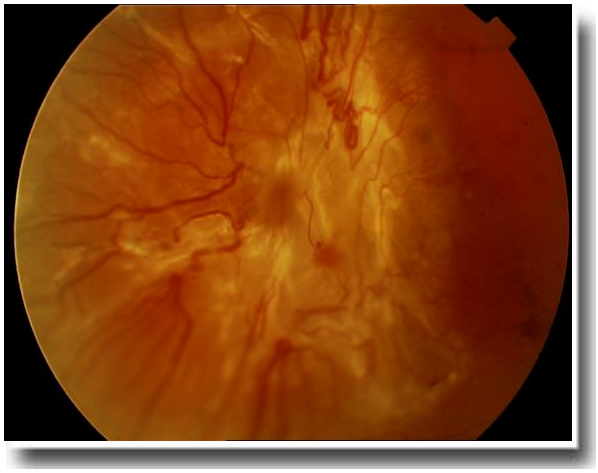

Fig. 3. Retinal neovascularization with the formation of new small-caliber vessels and capillary proliferation. Hematoxylin and eosin staining. ×200.

*3.6. Combined lesions and risk factors*

Simultaneous damage to multiple target organs was detected in a significant proportion of patients: nephropathy and retinopathy in 29.6%, and multiple organ complications in 16.5%.

Table 3

Relationship between morphological changes and clinical parameters

| Morphological changes | Correlating parameter | r (Pearson) | p-value |
|---|---|---|---|
| β-cell degeneration | Duration of diabetes | 0,72 | < 0,001 |
| β-cell degeneration | HbA1c | 0,58 | < 0,01 |
| Mesangial dilation | Длительность СД | 0,74 | < 0,001 |
| Glomerular BM thickness | HbA1c | 0,66 | < 0,001 |
| Glomerulosclerosis | eGFR | -0,81 | < 0,001 |
| Retinal neovascularization | Длительность СД | 0,79 | < 0,001 |
| Pericyte loss | HbA1c | 0,71 | < 0,001 |
| Overall microangiopathy severity | HbA1c | 0,68 | < 0,01 |

**Discussion**

This study presents a comprehensive clinical and morphological analysis of diabetes mellitus in patients in the Republic of Uzbekistan and confirms the systemic nature of the disease, primarily affecting target organs—the pancreas, kidneys, and retina. The results demonstrate typical micro- and macroangiopathic changes consistent with data from the global literature, while also reflecting regional differences in the disease course.

*4.1. Epidemiological aspects*

The increasing prevalence of diabetes mellitus in Uzbekistan is consistent with global trends described by the WHO and the International Diabetes Federation [1, 2]. Despite the official registration of over 230,000 patients, calculation models indicate a significantly higher true prevalence of the disease, suggesting a large number of undiagnosed cases. Late detection of diabetes contributes to the development of complications already at the time of diagnosis, as evidenced by the high incidence of nephropathy and retinopathy in the study cohort.

*4.2. Morphological changes and pathogenesis*

Pancreatic β-cell degeneration, detected in most samples, reflects a progressive loss of functional islet mass. These changes are consistent with the pathogenetic mechanisms described in the Robbins & Cotran guidelines, including the influence of hyperglycemia, oxidative stress, and inflammatory mediators [6]. In type 1 diabetes, signs of autoimmune damage (insulitis) predominated, whereas in type 2 diabetes, glucotoxicity and lipotoxicity played a leading role.

Morphological changes in the kidneys were consistent with the classic picture of diabetic nephropathy. Severe glomerulosclerosis and thickening of the

basement membranes directly correlated with a decrease in eGFR, confirming the decisive role of structural damage in renal dysfunction. These data are consistent with the results of modern clinical reviews emphasizing the importance of morphological criteria in predicting renal failure in diabetes [4].

*4.3. Diabetic retinopathy as a manifestation of systemic microangiopathy*

Retinal neovascularization is a key morphological feature of proliferative diabetic retinopathy and reflects chronic retinal ischemia and activated angiogenesis, consistent with the recommendations of the International Council of Ophthalmology [5]. Pericyte loss and thickening of capillary basement membranes indicate early damage to the microvasculature and explain the development of microaneurysms, hemorrhages, and macular edema.

The high frequency of combined kidney and retinal damage confirms the systemic nature of diabetic microangiopathy and the common pathogenetic mechanisms underlying damage to various organs.

*4.4. The importance of glycemic control*

The pronounced correlation between HbA1c levels and the degree of morphological changes underscores the key role of glycemic control in preventing complications. The obtained data are consistent with the results of large international studies showing that lowering HbA1c significantly reduces the risk of developing microvascular lesions. The high proportion of patients with inadequate glycemic control indicates the need to optimize therapeutic strategies and improve treatment adherence.

*4.5. Study limitations*

The main limitations of the study include its cross-sectional design, the lack of a control group, and the limited amount of pancreatic morphological material. Furthermore, the study was conducted at a specialized center, which may have resulted in the inclusion of more severe clinical cases.

**Conclusion**

Diabetes mellitus is one of the most significant medical and social problems in the Republic of Uzbekistan, characterized by a high prevalence and complication rate. This study demonstrated that the disease is accompanied by pronounced clinical and morphological changes, primarily affecting the pancreas, kidneys, and retina.

The main histopathological manifestations of diabetes mellitus include degeneration of β-cells in the islets of Langerhans with fibrous replacement, glomerulosclerosis with thickening of the glomerular basement membranes, and microangiopathic changes in the retina with the development of neovascularization. The severity of these changes is closely related to the level of glycemic control and the duration of the disease.

These findings highlight the key role of early diagnosis and maintenance of stable metabolic control in preventing irreversible target organ damage and reducing the risk of severe diabetic complications.

**Prospects for further research**

Promising areas for further research include multicenter prospective observations using immunohistochemical and molecular methods aimed at studying the pathogenetic mechanisms of diabetic complications and developing personalized therapeutic approaches.

**Information on conflict of interest**

There are no potential or apparent conflicts of interest related to this manuscript at the time of publication, and are not anticipated.

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**Аллабердієв Б.Т., Ахрарова А.Б. Актуальність цукрового діабету, епідеміологічна ситуація та клініко-морфологічні особливості в Республіці Узбекистан.**

**Ташкентський державний медичний університет, Ташкент, Республіка Узбекистан.**

**РЕФЕРАТ. Актуальність.** Цукровий діабет (ЦД) є одним з найпоширеніших хронічних ендокринних захворювань, що характеризується стійкою гіперглікемією та розвитком мікро- та макро-ангіопатичних ускладнень. Незважаючи на зростання захворюваності, дані про клініко-морфологічні особливості ЦД у країнах Центральної Азії, включаючи Республіку Узбекистан, залишаються обмеженими. **Мета.** Проаналізувати клінічні та морфологічні особливості цукрового діабету у пацієнтів Республіки Узбекистан, а також оцінити взаємозв'язок між гістопатологічними змінами та клінічними проявами захворювання. **Методи.** Проведено одномоментне описове дослідження 230 пацієнтів із ЦД 1-го та 2-го типів, що спостерігалися у 2022–2024 роках. Оцінювалися клінічні, біохімічні та інструментальні показники, включаючи рівень глікемії, HbA1c, функцію нирок та стан органу зору. Морфологічний аналіз виконувався на зразках підшлункової залози, нирок та сітківки, отриманих при аутопсії та прижиттєвої біопсії нирки. Використовувалися стандартні гістологічні методи фарбування та морфометричний аналіз. Статистична обробка проводилася із застосуванням кореляційного та порівняльного аналізу. **Результати.** Недостатній глікемічний контроль (HbA1c > 7%) виявлено у 92,2% пацієнтів. Морфологічне дослідження показало дегенерацію β-клітин острівців Лангерганса з фіброзним заміщенням, виражений гломерулосклероз та ознаки діабетичної ретинопатії з неоваскуляризацією. Ступінь морфологічних змін достовірно корелювала з тривалістю захворювання та рівнем HbA1c ($p<0,01$). У значної частини пацієнтів відзначалося поєднане ураження кількох органів-мішеней. **Висновок.** Цукровий діабет в Республіці Узбекистан характеризується вираженими клініко-морфологічними змінами, що тісно пов'язані з недостатнім глікемічним контролем та тривалістю захворювання. Отримані дані наголошують на необхідності ранньої діагностики та оптимізації терапії для профілактики прогресування ускладнень.

**Ключові слова:** цукровий діабет, морфологія, діабетична нефропатія, діабетична ретинопатія, β-клітини, мікроангіопатія.