The Bioscan AN INTERNATIONAL QUARTERLY JOURNAL OF LIFE SCIENCES
21(2): S.I (2), 1937-1946, 2026 www.thebioscan.com

PROGNOSTIC VALUE OF NEPHRINE AS THE EARLY MARKER OF DIABETIC NEPHROPATHY IN PATIENTS WITH TYPE 1 DIABETES MELLITUS

Z.A. Rakhimberdieva[1]* B.Kh. Shagazatova[2], Alimova N.U[3], Rakhimova M.E.[4]
[1]rakhimberdieva90@mail.ru,
[2]shagazatova@gnail.com,. Uzbekistan, Tashkent city. Tashkent State Medical University Department of Internal Disease, endocrinology.
[3] alimova_ali@mail.ru Uzbekistan, Tashkent city. Republican Specialized Scientific and Practical Center for Endocrinology. Department of Pediatric Endocrinology.
[4]Tashkent State Medical University Department of Internal Diseases in Family Medicine No. 2.

DOI:https://doi.org/10.63001/tbs.2026.v21.i02.S.I(2).pp1937-1946

Keywords:
diabetes mellitus,
diabetic nephropathy,
nephrin.
.
.
Received on:
18-05-2026
Accepted on:
06-06-2026
Published on:
16-06-2026

Abstract

BACKGROUND: As per the Diabetic Atlas published by the International Diabetes Federation, 10th edition, 2021, the total number of patients with diabetes in the world is 537 million people.
OBJECTIVES: To investigate the efficacy of nephrin as an early biomarker for diabetic nephropathy in individuals with type 1 diabetes.
METHODS. To investigate the early diabetic nephropathy marker, we analyzed 80 ill children with type 1 diabetes from the Uzbek community at the nephropathy stage for the existence of nephrinemia in their blood. To identify deviations from the norm in children with type 1 diabetes and compare the indicators of biochemical and enzyme immunoassays, we studied a control group consisting of 16 healthy children of the appropriate age and gender
RESULTS. According to the instructions of the reagent for determining the level of nephrin, the normal values in the blood serum are 0.118–0.65 ng/ml. The concentration of nephrin measured in the blood serum of individuals with type 1 diabetes in the NAU stage was 0.65 ± 0.06; this was significantly higher than its indicators in the control group – 0.018± 0.08; ($p < 0.001$). In general, an increased level of nephrin was detected in 32.5% of all examined patients with type 1 diabetes.
CONCLUSION. The assessment of nephrin levels in the blood serum of pediatric patients with type 1 diabetes at the NAU stage revealed a value of 0.65 ± 0.06, which is markedly elevated compared to the control group – 0.018± 0.08; ($p < 0.001$).

BACKGROUND

«To date, diabetes mellitus, which has the scale of non-infectious epidemic of the XXI century, is considered one of the most common diseases among the children and adolescents. The International Diabetes Federation's Diabetic Atlas, 10th edition, 2021»[1], reports that the global population of individuals with diabetes is 537 million. By 2030, the population of individuals with diabetes mellitus is anticipated to surpass 643 million. The population of individuals with type 1 diabetes aged under 19 has risen to 1.2 million. From 2000 to 2016, the National Register indicates that the incidence of type 1 diabetes among children in Uzbekistan rose from 7.5 to 19.8 per 100,000, but death declined to 99%, maintaining consistent morbidity rates. «From 2000 to 2016, the prevalence of type 1 diabetes among children and adolescents aged 0 to 14 years was 12.7 per 100,000 individuals. In the Republic of Uzbekistan, the incidence of type 1 diabetes among children aged 0-14 years has risen by an average of 2.6 times during a span of 16 years»[2]. The prevalence of type 1 diabetes among youngsters in the Republic of Uzbekistan is on the rise. In recent years, the incidence of newly diagnosed type 1 diabetes in children under 5 years has risen from 7.8% to 12.3%, indicating

an escalation in instances of the illness at a younger age in Uzbekistan. The frequency of T1DM among females of this age should be emphasized [2]

«A significant clinical characteristic of diabetes is its correlation with chronic tissue problems. The transient elevation in hyperglycemia does not result in significant clinical consequences. The length and severity of hyperglycemia are the primary causative factors in the onset of organ damage. Initial morphological indicators of renal impairment include nephromegaly and altered dopplerography; however, the extent of damage is most accurately assessed by proteinuria and glomerular filtration rate (GFR)»[3]. «Clinical and epidemiological investigations of children and adolescents with type 1 diabetes in Tashkent and five areas of Uzbekistan determined the prevalence of chronic kidney disease (CKD) to be 19.4% in children and 35.5% in adolescents»[4]. «The typical incidence of diabetic nephropathy is elevated at 3% year throughout the first 10 to 20 years after the beginning of diabetes. Typically, it takes 15 years to inflict damage on tiny blood arteries in organs like the kidneys, eyes, and nerves. It is estimated that over 20% and up to 40% of diabetic patients will develop chronic kidney disease (CKD)»[6,7], «varying by population, while a considerable number progress to end-stage kidney disease, necessitating renal replacement therapies such as kidney transplantation. Diabetes devoid of clinical indicators of renal impairment throughout the first 20-25 years is much less probable (1% year) to result in severe renal problems in later life» [5].

«Nephrin, or Nphs1, is an adhesion protein located in the intercellular junctions of podocytes within the glomerulus. Studies demonstrate a decrease in nephrin expression in many proteinuric kidney disorders and in animal models of glomerular disease. The reduction in nephrin expression is thought to precede podocyte loss and correlates with the advancement of kidney disease»[8, 9, 10, 11].

As diabetic nephropathy (DN) advances, there is a progressive decline in podocyte quantity and a loss of foot processes, mostly attributable to apoptosis or podocyte shedding. «Thus, urinary podocytes and their particular proteins are regarded as possible biomarkers for detecting podocyte damage. This has initiated inquiries into innovative biomarkers for the early identification of diabetic nephropathy (DN). At now, the emphasis is on assessing novel and more specific urinary indicators that emerge before the start of microalbuminuria, particularly podocyte-specific protein products, due to the difficulties associated with the direct detection of urinary podocytes»[8, 9, 10, 11].

«Recent research has focused on the significance of various podocyte proteins, including nephrin, podocalyxin, synaptopodin, podocin, and mindin, in the early identification of diabetic nephropathy (DN). Nephrin has emerged as the most promising urine biomarker for the early identification of diabetic nephropathy (DN)»[12].

OBJECTIVES

To assess the effectiveness of nephrin as an early indicator of diabetic nephropathy in individuals with type 1 diabetes.

METHODS

A randomized, longitudinal, observational study was conducted at a single center.

Criteria for inclusion and exclusion in T1DM:

Inclusion criteria:

1. Children diagnosed with type 1 diabetes
2. In the NAU stage
3. Between the ages of 1 and 14 years

Exclusion criteria:

1. Children with type 1 diabetes, complicated by severe stages of diabetic nephropathy and CKD, retinopathy, diabetic foot;
2. Type 1 diabetes with concomitant endocrine diseases and type 1 diabetes in patients older than 14 years.

Eligibility criteria for the healthy control group.

Inclusion criteria:

Inclusion Criteria:

1. No previously diagnosed carbohydrate metabolism disorders.

2. Age range between 1 and 14 years.

Exclusion Criteria:

1. Severe renal insufficiency or existing inflammatory kidney diseases.

2. History of oncological or autoimmune kidney diseases.

3. Nephrin levels exceeding the reference range (>0.65 ng/ml).

4. Presence of carbohydrate metabolism disorders (HbA1c > 5.8%).

Study Conditions

The research was conducted at the Republican Specialized Scientific and Practical Center of Endocrinology, within the Department of Pediatric Endocrinology, following the established inclusion criteria and with signed informed consent.

Study Duration

The study took place from September 2018 to September 2021.

Medical Intervention Description

Blood samples were collected from the peripheral vein of all participants for biochemical analysis, including nephrin measurement. Clinical and laboratory data were evaluated, including the age at diabetes onset, duration of type 1 diabetes, and HbA1c levels.

Main Outcome of the Study

The evaluation of nephrin levels in the blood serum of pediatric and adolescent patients with type 1 diabetes at the NAU stage showed a value of 0.65 ± 0.06, which is significantly higher than that of the control group (0.018 ± 0.08; $p < 0.001$).

Additional Study Outcomes

A correlation was identified between nephrin levels and the onset of the disease in children aged 1 to 5 years.

Subgroup Analysis

Patients were categorized into three groups based on disease duration:

1.1 to 5 years

2. 5 to 10 years

3.More than 10 years

Additionally, participants were divided into two groups according to nephrin levels: those with normal nephrin levels and those with elevated nephrin levels.

Methods of outcomes registartion

Nephrin was determined by enzyme immunoassay in microplate format on the automatic "ELISA" device (USA). Normal values of nephrin in blood serum were considered 0.118–0.65 ng/ml.

Methods of statistical data analysis.

The methods of mathematical statistics were used in the statistical processing of clinical material. In particular, methods of frequency analysis (%, $\chi 2$), Methods of statistical analysis included variation statistics (arithmetic mean (M), standard deviation (σ), standard error (m), etc.), variance analysis (t-test), and correlation analysis (pairwise correlation coefficient r). Clinical data were processed using the STATISTICA 10.0 software package.

RESULTS

Subjects of the research.

The study included 80 individuals with type 1 diabetes (DM1) aged 1 to 14 years, consisting of 39 males and 41 females. The average age of the patients was 10 years, with a mean age of diabetes onset at 8 years. The control group comprised 16 healthy individuals (without glucose metabolism disorders) aged 1 to 14 years, including 9 males and 7 females.

The diagnosis of type 1 diabetes (DM1) was established according to the 2019 WHO recommendations and criteria. Among the patients, 54 (67.5%) had normal nephrin levels, while 26 (32.5%) exhibited elevated nephrin levels.

The serum nephrin levels in individuals with type 1 diabetes were examined as an early indicator of diabetic nephropathy. The reagent instructions indicate that the normal serum nephrin levels range from 0.118 to 0.65 ng/ml. The nephrin level measured in the blood serum of

patients with type 1 diabetes at the NAU stage was 0.65 ± 0.06, considerably above the control group's value of 0.018 ± 0.08 ($p < 0.001$). Overall, increased nephrin levels were seen in 32.5% of all assessed individuals with type 1 diabetes, averaging 1.13 ± 0.10. Table 1 The study's findings indicated a correlation between the length of type 1 diabetes and elevated nephrin levels: 0.63 ± 0.09 for a disease duration of 1 to 5 years; 0.64 ± 0.09 for 5 to 10 years; and 0.72 ± 0.08 for over 10 years. Table 2 The analysis of the results indicated that the prevalence of children and adolescents with type 1 diabetes exhibiting normal nephrin levels was Higher prevalence was observed in the cohort with disease onset between 5 and 10 years (37%). In contrast, a greater proportion of patients with diabetes onset between 1 and 5 years exhibited elevated nephrin levels (46.2%). Among children and adolescents with type 1 diabetes exhibiting normal nephrin levels, there is a significantly greater number of patients with a disease duration of 1 to 5 years, whereas in the cohort with elevated nephrin levels, a higher percentage of patients has a disease duration of 5 to 10 years. Analysis of the degree of diabetes compensation and nephrin levels in the blood of children and adolescents revealed no significant difference in the number of patients with normal and elevated nephrin levels between the well-controlled and poorly controlled type 1 diabetes groups. In the well-controlled group, the percentages of patients with normal and elevated nephrin levels were 20.4% and 19.2%, respectively; in the poorly controlled group, these percentages were 79.6% and 80.8%, respectively. Overall, individuals with poorly managed diabetes mellitus were considerably more prevalent in both groups. (Table 4) Clinical and laboratory studies indicate that in children and adolescents with type 1 diabetes, there is a tendency for a slight decline in carbohydrate and lipid metabolism indicators, as well as creatinine and urea levels in the blood, correlated with nephrin levels; however, no such relationship was observed in blood pressure or BMI parameters in either group. Overall, clinical and laboratory indicators between the groups with normal and high nephrin levels in the blood did not exhibit significant differences. (Table 5) The investigation of biochemical and hemodynamic parameters, together with lipid and carbohydrate metabolism data in patients with NAU and normal nephrin levels after one year, indicated no significant alterations from the baseline data. We investigated the dynamics of individuals with high nephrin levels; thus, a year later, we conducted a re-analysis of several biochemical markers, hemodynamic metrics, and lipid metabolism data. The findings indicated a notable elevation in microalbuminuria, systolic blood pressure (SBP), and diastolic blood pressure (DBP), with a considerable reduction in glomerular filtration rate (GFR). In 38% of individuals with higher nephrin levels, microalbuminuria (MAU) was identified after one year. (table 6)

Table 1

Indicators of the nephrin level in the blood serum of sick children with type 1 diabetes

Group study	Nephrin index, ng/ml
Healthy individuals, n=16	0,018±0,08
with type 1 DM (NAU), n=80	0,65±0,06*

*Note: The data is presented in the form of the mean value and standard deviation. Frequency indices are i ndicated as a percentage of the total number of patients in this group. *P<0.001 – the reli ability of differences between healthy individuals and patients with type 1 diabetes with N AU.*

Table 2

Serum nephrin levels in individuals with type 1 diabetes relative to disease duration

Duration of type 1 DM	Mean value of nephrin
from 1 to 5 years old	0,63±0,09
from 5 to 10 years old	0,64±0,09
≥ 10 years old	0,72±0,08

Note:

Table 3

Distribution of children and adolescents with type 1 diabetes in the NAU cohort with normal and high nephrin levels, based on the age of illness start and its duration

	NAU stage, n=80					
	Patients with normal nephrin levels, n=54		Patients with elevated nephrin levels, n=26		χ^2	P
	abs.	%	abs.	%		
Age of onset of the disease						
from 1 to 5 years old	20	37,0	12	46,2	0,61	>0,05
from 5 to 10 years old	26	48,1	10	38,5	0,67	>0,05
≥10 years old	8	14,8	4	15,4	0,00	>0,05
Duration of the disease						
from 1 to 5 years old	42	77,8	10	38,5	11,92	<0,001
from 5 to 10 years old	12	22,2	16	61,5	11,92	<0,001

Table 4

Indicators of diabetes compensation and blood nephrin levels in infants and teenagers with type 1 diabetes and NAU

Indices	NAU stage, n=80					
	Patients with normal nephrin levels n=54		Patients with elevated nephrin levels n=26		χ^2	P
	abs.	%	abs.	%		
HbA1c≤7,0%	11	20,4	5	19,2	0,01	>0,05
HbA1c>7,0%	43	79,6	21	80,8	0,01	>0,05

Table 5

Clinical and laboratory parameters of children and adolescents with type 1 diabetes based on nephrin levels.

Indices	Стадия NAU, n=80			
	Patients with normal nephrin levels, n=54	**Patients with elevated nephrin levels, n=26**	**t**	**P**
GFR	80,3±2,14	82,7±1,78	0,86	>0,05
Creatinine	64,8±1,06	66,8±2,06	0,86	>0,05
Urea	5,29±0,27	5,39±0,27	0,26	>0,05
Average glycemic profile	9,08±0,30	9,69±0,65	0,85	>0,05
HbA1c, %	9,59±0,33	9,78±0,55	0,30	>0,05
Total cholesterol, mmol/l	3,48±0,12	3,72±0,1	1,54	>0,05
Triglycerides, mmol/l	0,79±0,08	0,81±0,09	0,17	>0,05
Microalbumin	11,1±0,39	11,1±0,39	0,00	>0,05
SBP (systolic blood pressure)	98,7 ± 0,99	97,7 ± 0,99	0,71	>0,05
DBP (diastolic blood pressure)	64,3 ± 0,74	64,5 ± 0,75	0,19	>0,05
Heart rate	87,6 ± 1,48	89,6 ± 1,57	0,93	>0,05
BMI kg/m^2	16,8±0,35	17,3±0,58	0,74	>0,05

Table 6

Biochemical and hemodynamic parameters of patients with elevated nephrin levels after 1 year

Indices	Group of patients with elevated nephrin levelsn=26	A group of patients with elevated nephrin levels after 1 yearn=26
Creatinine	66,8±2,06	72,9±4,53
Urea	5,39±0,27	5,7±0,28
GFR	82,7±1,78	73,1±1,98*
Microalbumin	11,1±0,39	85±2,52*
SBP	97,7 ± 0,99	101,7± 0,89*
DBP	64,5 ± 0,75	70,8±0,58*
Heart rate	89,6 ± 1,57	88,7±1,67
HbA1c, %	9,78±0,55	9,8±0,56
Total cholesterol, mmol/l	3,72±0,1	4,06±0,12
Triglycerides, mmol/l	0,81±0,09	0,82±0,05

Note: - the differences with respect to the data of the group of patients with elevated nephrin levels are significant (- P<0,05, * - P<0,001)*

Summary of the Main Study Result

The assessment of nephrin levels in the blood serum of children and adolescents with type 1 diabetes at the NAU stage revealed a value of 0.65 ± 0.06, significantly higher than the control group's 0.018 ± 0.08 ($p < 0.001$). Among the patients examined at the NAU stage, 32.5% had higher nephrin levels, particularly correlated with illness start between the ages of 1 and 5 years.

Discussion

Recent clinical and experimental research have shown a significant link between the rise in albuminuria (AU) and the functional and ultrastructural abnormalities in podocytes [13, 14]. These findings suggest that these changes can occur prior to the detection of microalbuminuria (MAU) and can even manifest with a brief duration of diabetes mellitus (DM). [15]. This evidence underscores the early engagement of podocytes in the initiation of renal impairment in diabetes mellitus, prompting a heightened interest in these cells for the development of effective preclinical diagnostic methods and strategies for inhibiting diabetic nephropathy (DN). Under normal conditions, the intricate architecture of podocytes allows them to carry out a wide array of functions, displaying adaptability. However, this also renders these cells highly susceptible to damage. When subjected to various harmful influences such as toxic, metabolic, and hemodynamic factors, podocytes undergo both functional and structural changes, a condition termed "podocytopathy." [16]. These signs of podocytopathy include the smoothing of podocyte processes, which leads to a compromised permeability of the slit diaphragm. Moreover, apoptosis, enlargement, detachment of podocytes from the glomerular basement membrane leading to exfoliation into the urinary space, and the presence of intact cells and structural proteins in the urine are noted. Moreover, a decrease in the quantity of podocytes inside the glomerulus, known as podocytopenia, is evident.

The glomerular filter is comprised of three layers: the glomerular basement membrane, the vascular endothelium, and the slit diaphragm found between the podocyte foot processes. While previously, the condition of the basement membranes of glomerular capillaries was believed to be the main factor in the onset of proteinuria, it is now clear that the role of podocyte proteins is significant [17]. In most cases, glomerular damage is now acknowledged as a podocyte pathology, which is partly due to alterations in podocytic protein genes. The slit diaphragm, a key component for maintaining the function and structure of the filtration barrier, acts as a specialized intercellular connection between adjacent podocyte foot processes. It consists of a complex multi-protein signaling assembly that actively manages the architecture of the podocyte pedicel by transmitting signals to the actin of the cytoskeleton. This signal assembly encompasses signal adapters, structural proteins, receptors, additional supporting proteins, and ion channels. Furthermore, it is essential for regulating other biological functions of the podocyte, including endocytosis, organization of the cytoskeleton, differentiation, suppression of proliferation, and podocyte viability. Nephrin, a product of the NPHS1 gene, is a significant structural protein of the slit filtration diaphragm, belonging to the adhesive proteins of the immunoglobulin superfamily, with a molecular mass of 160 kDa. Alterations in both the structure of nephrin itself and the associated protein complex precede disruptions in podocyte architecture, leading to smoothing of the podocyte processes and the onset of proteinuria. [18]. Research indicates that urinary nephrin levels may function as a measure for podocyte dysfunction in individuals with chronic glomerulonephritis. This assessment facilitates the evaluation of disease activity, the degree of podocytic dysfunction, and the prediction of response to immunosuppressive medication [17].

In our scientific work on the determination and study of nephrin in blood serum, we examined 80 sick children and adolescents with T1DM in the NAU stage. In the future, we divided them into 2 groups – with normal and elevated levels of nephrin. The result obtained by us for determining the level of nephrin in the blood serum of patients with T1DM in the NAU stage was 0.65± 0.06; which significantly exceeded its values in the control group of 0.018± 0.08; ($p <0.001$). In general, elevated nephrin levels were detected in 32.5% of

all examined T1DM patients and amounted to 1.13±0.10; and in 67.5% of patients, this value turned out to be 0.35 ± 0.02. The findings of the research revealed a tendency to increase the level of nephrin with a longer duration of T1DM: with the duration of this disease from 1 to 5 years, this indicator was 0.63 ± 0.09; 0.64 ± 0.09 – with a duration of 5 to 10 years; 0.72 ± 0.08 – more than 10 years. There were no gender differences in the groups with normal and elevated nephrin levels.

The examination of the age at disease onset reveals that the majority of children and adolescents with Type 1 Diabetes Mellitus (T1DM) were found in the cohort with normal nephrin levels, specifically between the ages of 5 to 10 years (37%). Conversely, in the cohort with elevated nephrin levels, the highest percentage of patients (46.2%) was identified among children who developed diabetes between the ages of 1 to 5 years. This confirms that nephrin levels act as an early marker of kidney dysfunction in individuals with type 1 diabetes mellitus.

The findings regarding the impact of T1DM disease duration in children and adolescents on nephrin levels indicated that patients with normal nephrin levels predominantly had a disease duration of 1 to 5 years. Conversely, in the cohort with elevated nephrin levels, there was a significantly higher prevalence of patients with a disease duration of 5 to 10 years compared to those with normal nephrin levels.

Clinical and laboratory indicators of carbohydrate, lipid metabolism, creatinine and urea data, as well as the results of measuring blood pressure, BMI of both groups, i.e. with normal and elevated nephrin levels, did not differ significantly. This research aimed to investigate the correlation between nephrin levels and several laboratory markers. Statistically significant relationships were seen with microalbuminuria (r=0.74, p=0.001), creatinine (r=0.43, p=0.003), and GFR (r=-0.16, p=0.03). Irena Kostowska's research [19] revealed that 82% of individuals with normoalbuminuria had elevated nephrin concentrations in urine. In the microalbuminuria subgroup, 88% of individuals had higher nephrin levels in urine, while in the macroalbuminuria subgroup, this number was 100%. Similar to our research on the works of Irina Kostowska, the concentration of nephrin in urine exhibited a negative correlation with GFR.

We were interested in the dynamics of the condition of patients with elevated nephrin levels, and therefore, a year later, a re-analysis of a number of biochemical parameters, hemodynamic parameters and lipid metabolism data was carried out. The results showed a significant increase in microalbuminuria, SHP and DHP, and there was also a significant decrease in GFR. The analysis of the morphofunctional condition of the kidneys over one year in subjects with high nephrin levels indicated that 38% of infants and adolescents with T1DM had microalbuminuria (MAU).

Therefore, the determination of the level of nephrin gives reason to use it as the early marker in the diagnosis of DN.

CONCLUSION

The assessment of nephrin levels in the blood serum of pediatric and teenage patients with type 1 diabetes at the NAU stage revealed a value of 0.65 ± 0.06, which is markedly elevated compared to the control group at 0.018 ± 0.08 ($p < 0.001$). In the assessed individuals at the NAU stage, 32.5% had an increased nephrin level, particularly correlated with illness start between the ages of 1 and 5 years.

Examination of the outcomes of the morphofunctional state of the kidneys in dynamics after a year among children and adolescents with T1DM with elevated nephrin levels revealed the presence of MAU in 38%. Therefore, there is a reason to use the determination of the level of nephrin as an early marker in the diagnosis of DN.

REFERENCES

1. IDF 2021 10 th Edition.
2. Rakhimova G.N., Alimova N.U. Monitoring of epidemiological indicators of type 1 diabetes mellitus in children and adolescents according to the national register from 2000 to 2011 in Uzbekistan // Scientific and practical

journal "Pediatrics", 2015, No. 3, pp.164-167.

3. Zhang J, Liu J, Qin X. Advances in early biomarkers of diabetic nephropathy.RevAssocMedBras. 2018;64(1):85–92. doi: 10.1590/1806-9282.64.01.85. [PubMed] [CrossRef] [GoogleScholar]
4. 4. Rakhimova G.N., Sadikova A.S. Optimization of criteria for diagnosis, prevention and treatment of chronic kidney disease in children and adolescents with type 1 diabetes mellitus. Methodological recommendations. Tashkent, 2018. - p.38.
5. Magee C, Grieve DJ, Watson CJ, Brazil DP. Diabetic nephropathy: a tangled web to unweave. Cardiovasc Drugs Ther. 2017;31(5–6):579–592. doi: 10.1007/s10557-017-6755-9. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
6. Papadopoulou-Marketou N, Paschou SA, Marketos N, Adamidi S, Adamidis S, Kanaka-Gantenbein C. Diabetic nephropathy in type 1 diabetes. Minerva Med. 2018;109(3):218–228. [PubMed] [Google Scholar]
7. Nelson RG, Bennett PH, Beck GJ, et al. Diabetic Renal Disease Study Group: development and progression of renal disease in Pima Indians with non-insulin dependent diabetes mellitus. N Engl J Med. 1996;335:1636–1642. doi: 10.1056/NEJM199611283352203. [PubMed] [CrossRef] [Google Scholar]
8. Ünüvar S, Tanriverd Z, Aslanhan H. Potential prognostic role of immune system activation marker neopterin in patients with type 2 diabetes. J Med Biochem. 2018;37(4):465. doi: 10.2478/jomb-2018-0004. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
9. Nauta F L, Boertien W E, Bakker S J L, van Goor H, van Oeveren W, de Jong P E, Bilo H, Gansevoort R T. Glomerular and Tubular Damage Markers Are Elevated in Patients with Diabetes. Diabetes Care. 2011;34(4):975. doi: 10.2337/dc10-1545. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
10. Gatua W K, Makumi J N, Njagi E M. Evaluation of Urinary Tubular Enzymes as Screening Markers of Renal Dysfunction in Patients Suffering from Diabetes Mellitus Asian J Med Sci. 2011;3(3):84. [Google Scholar]
11. Kandasamy Y, Smith R, Lumbers E R, Rudd D. Nephrin: A biomarker of early glomerular injury. Biomarker Research. 2014;2(1):21. doi: 10.1186/2050-7771-2-21. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
12. Weil J E, Lemley K V, Mason C C, Yee B, Jones L I, Blouch K, Lovato T, Richardson M, Myers B D, Nelson R G. Podocyte detachment and reduced glomerular capillary endothelial fenestration promote kidney disease in type 2 diabetic nephropathy. Kidney Int. 2012;82(9):1010. doi: 10.1038/ki.2012.234. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
13. Reddy GR, Kotlyarevska K, Ransom RF. The podocyte and diabetes mellitus: is the podocyte key to the origins of diabetic nephropathy? CurrOpinNephrolHypertens 2008; 17: 32-36.
14. Stitt-Cavanagh E, MacLeod L, Kennedy CRJ. The podocyte in diabetic kidney disease. The Scientific World Journal 2009; 9:1127-1139
15. Pätäri A, Forsblom C, Havana M, Taipale H, Groop PH, Holthöfer H. Nephrineuria in diabetic nephropathy of type 1 diabetes. Diabetes. 2003;52(12):2969–2974.
16. Diez-Sampedro A, Lenz O, Fornoni A. Podocytopathy in diabetes: a metabolic and endocrine disorder. Am J Kidney Dis 2011; 58(4): 637-646.
17. Shchukina A.A., Bobkova I.N., Shestakova M.V., Vikulova O.K. Urinary excretion of markers of

hepatocyte damage in patients with diabetes mellitus. Therapeutic Archive. 2015. No. 10. pp. 62-66. 2015. No. 10. pp. 62-66.

18. Immunochemical analysis in laboratory medicine. Textbook /edited by V.V. Dolgov. M.-Tver: LLC "Publishing House "Triada", 2015. p.418
19. Kostovska I, Tosheska-Trajkovska K, Topuzovska S, Cekovska S, Spasovski G, Kostovski O, Labudovic D. Urinary nephrine is earlier, more sensitive and specific marker of diabetic nephropathy than microalbuminuria. J Med Biochem. 2020 Jan 10;39(1):83-90. doi: 10.2478/jomb-2019-0026. PMID: 32549781; PMCID: PMC7282240.