General clinical and anthropometric parameters in patients with type 1 diabetes mellitus depending on the level of albumin in the urine

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Currently there are many experimental markers of diabetic nephropathy, but clinical practice focuses mainly on the presence of albuminuria, which usually manifests itself in both adults and children on average 5-7 years after the onset of diabetes. The aim of the study was to study the general clinical and anthropometric parameters in patients with type 1 diabetes mellitus (T1D) depending on the level of albumin in the urine. The study included 78 men and 62 women aged 22 to 26 years with T1D. The control group consisted of 8 healthy men and 13 healthy women of the same age. The level of microalbuminuria was determined in all patients by enzyme-linked immunosorbent assay. The assessment of general clinical (pulse, systolic, diastolic pressure) and anthropometric (height, weight, body surface area, waist circumference, body mass index) indicators was performed. Statistical processing of the obtained results was performed in the license package "Statistica 5.5" using non-parametric evaluation methods. It was found that angio-, retino- and neuropathy occurred in all patients with T1D. Simultaneously with the increase in albuminuria, the percentage of patients with deeper degrees of these complications increased. It was found that with increasing levels of albumin in the urine in most cases increases the percentage of patients with a correspondingly severe degree of these complications. Thus, in patients with T1D men found: angiopathy of the III degree with normoalbuminuria - 12.5 %, with microalbuminuria - 40.0 %, with proteinuria - 53.8 %, retinopathy of the II-III degree with normoalbuminuria - 0 % and 7.5 %, with microalbuminuria - 4.0 % and 40.0 %, with proteinuria - 100 % and 0 %; II-III degree neuropathy with normoalbuminuria - 65.0 % and 0 %, with microalbuminuria - 92.0 % and 0 %, with proteinuria - 0 % and 92.3 %. In patients with T1D women were found: angiopathy of the III degree with normoalbuminuria - 29.0 %, with microalbuminuria - 13.0 %, with proteinuria - 62.5 %; retinopathy of the II-III degree with normoalbuminuria - 3.2 % and 9.7 %, with microalbuminuria - 4.3 % and 26.1 %, with proteinuria - 87.5 % and 0 %; II-III degree neuropathy with normoalbuminuria - 71.0 % and 0 %, with microalbuminuria - 91.3 % and 0 %, with proteinuria - 12.5 % and 75.0 %. In patients with T1D with normo-, microalbuminuria and proteinuria, the value of systolic, diastolic blood pressure and pulse, in most cases, significantly higher than in healthy subjects (respectively in men by 6.1-18.3 % - 3.6-20.3 % and 4.2-14.7 %; in women - by 5.0-20.0 % - 9.1-22.8 % and 8.0-31.6 %). The value of these indicators increased with the increase in the level of albumin in the urine (respectively in men by 11.4 % - 16.1 % and 10.1 %; in women -- by 13.3 % - 10.0 % and 21.8 %). Patients with T1D had lower values of growth (respectively in men by 6.1-18.3 % - 3.6-20.3 % and 4.2-14.7 %; in women - by 5.0-20.0 % - 9.1-22.8 % and 8.0-31.6 %). The value of these indicators increased with the increase in the level of albumin in the urine (respectively in men by 11.4 % - 16.1 % and 10.1 %; in women -- by 13.3 % - 10.0 % and 21.8 %). Patients with T1D had lower values of growth (respectively in men by 4.6-9.2 %; in women - 2.2-4.1 %), weight (only in men by 9.0-26.4 %) and body surface area (respectively in men by 7.2-17.7 %, in women - 4.8 % only in the group of proteinuria). Body mass index in sick men, compared with healthy, was significantly lower only in the group of proteinuria (by 3.5 %); and in women it was higher in the groups of normo- and microalbuminuria (by 10.6 % and 11.2 %). Patients with T1D women compared to healthy women had a larger waist circumference (by 5.5-11.8 %), and in patients with T1D men - on the contrary, this figure was lower in the group of microalbuminuria (by 4.0 %). Thus, the differences in general clinical and anthropometric parameters between patients with
**Introduction**

Currently, about 380 million people worldwide suffer from diabetes and it is projected that by 2035 this figure will double [8, 15, 16]. The important social significance of this pathology is that it leads to early disability and mortality due to the development of the following vascular complications: retinopathy, diabetic nephropathy, diabetic foot, gangrene of the lower extremities, myocardial infarction, arterial hypertension, neuropathy, etc.

There are certain risk factors for the onset and progression of complications of diabetes. These include: nephropathy, the degree of compensation of carbohydrate metabolism, genetic predisposition, hypertension. Clinical and epidemiological studies have established the relationship between certain hemodynamic, metabolic, biochemical changes, duration of diabetes, severity and development of microangiopathies. A number of studies have described a graded relationship between albuminuria and the risks of adverse effects on the cardiovascular system and kidneys in patients with type 1 diabetes (T1D) [5, 23].

It is well known that the consequence of persistent hyperglycemia is damage to the walls of the capillaries of the kidneys. Against the background of a gradual decrease in the activity of renal corpuscles progressive deterioration of the filtration capacity of the kidneys (chronic renal failure). This pathology is noted in 20-40 % of patients with diabetes. Quite often diabetic nephropathy develops after 10 years of diabetes [9].

However, this damage can be in the early stages of diabetes, and for a long time it can deepen without visible signs and manifestations. Typical symptoms of intoxication, such as icteric skin and eyeballs, develop in many patients only in the late stages of the disease. If the result is unfavorable, kidney function may stop. And the only way in this case to improve the patient's condition is dialysis or kidney transplantation [12].

Diabetic nephropathy can be detected in the early stages by biochemical examination of urine. The degree of albuminuria in this category of patients is used as an important independent marker of diabetes damage, to classify the severity of the disease, to determine when a patient should be referred to a nephrologist, and as a guide for choosing a treatment strategy. Since there is a genetic component in the genesis of T1D, along with biochemical indicators, anthropological methods are currently being actively developed to identify risk groups for the development of this disease and identify on their basis signs that undoubtedly have diagnostic value [11, 14].

The aim of the study was to study the general clinical and anthropometric parameters in patients with T1D depending on the level of albumin in the urine.

**Materials and methods**

The study included 78 men and 62 women aged 22 to 26 years, who have T1D and were patients of therapeutic departments № 1 and № 2 of Vinnytsia Regional Highly Specialized Endocrinology Center. The control group consisted of 8 healthy men and 13 healthy women of the same age.

All patients were tested for microalbuminuria by enzyme-linked immunosorbent assay using spectrophotometry (reagents from ORGenTec, Germany). Test principle: patient samples combined with anti-human albumin peroxidase conjugate are added to the wells of the microplate containing purified human albumin. Unconnected components were washed out. The enzyme substrate in the presence of bound conjugate is hydrolyzed to form a blue color. The reaction was stopped by the addition of acid, resulting in the formation of a yellow color. The intensity of this color is directly proportional to the concentration of albumin. Regulatory values of microalbumin in the set of reagents used - 0-25 μg/ml.

Diagnosis of vascular lesions of the lower extremities was made on the basis of determining the pulsation of the vessels of the lower extremities and the patient's subjective complaints of pain in the legs while walking, intermittent claudication, perishing cold in feet.

The condition of the vessels of the eye fundus was assessed by an ophthalmologist after medical dilation of the pupils by direct ophthalmoscopy. To diagnose diabetic vascular lesions of the fundus, the classification of E. Kohner, M. Porte (1992) was used, according to which the following stages of diabetic retinopathy are distinguished: Stage I - non-proliferative, Stage II - pre-proliferative, Stage III - proliferative.

Diabetic neuropathy was established by a neurologist in patients with characteristic subjective sensations in the form of numbness, paresthesia, seizures of the lower extremities, pain in the legs at rest, as well as on the basis of objective neurological examination data on pain, tactile, vibration, temperature sensitivity or reduction/loss of tendon reflexes.

Blood pressure was measured on the brachial artery according to the Korotkov method twice with a five-minute interval in a sitting position after a 30-minute rest. Average indicators were registered. Blood pressure measurements
were performed according to the recommendations of EHS experts (2007). ECG recording was performed according to the generally accepted method in 12 standard leads using a diagnostic automated system.

Anthropometric research included the determination of height, weight, body surface area, waist circumference and calculation of body mass index (BMI) (the ratio of body weight in kilograms to height in meters squared). Height was determined using a height meter (accuracy - up to 0.01 m) when the shoes were removed. Body weight was measured using medical scales (accuracy - up to 0.5 kg) without outer clothing in the morning. Waist circumference was measured with a centimeter tape. Normal body weight is considered at BMI 18.5-24.9 kg/m², excess at BMI 25.0-29.9 kg/m². Grade I obesity was diagnosed at BMI 30-34.9 kg/m², grade II obesity at BMI 35.0-39.9 kg/m².

Statistical data processing was performed in the license package "Statistica 5.5" using non-parametric methods of evaluation of the obtained results.

Results

Among patients with normoalbuminuria, a higher (\(p=0.092\)) percentage of men with absence of angiopathy and a lower (\(p=0.088\)) percentage with grade III angiopathy were found compared to women (30.0 %, 12.9 % and 12.5 %, 29.0 % respectively). Among patients with microalbuminuria, a higher (\(p<0.05\)) percentage of men with grade III angiopathy was found compared to women (40.0 % and 13.0 %, respectively). Significant or sex differences in the percentage of patients with angiopathy among patients with proteinuria have not been established (Fig. 1).

When comparing the frequency of absence or presence of angiopathy between men or women with different levels of albumin in the urine, it was found (see Fig. 1): in men - a higher (\(p<0.05\)) percentage with absence of angiopathy in the group with normoalbuminuria compared with microalbuminuria (respectively 30.0 % and 4.0 %); lower (\(p<0.05\) and \(p<0.01\)) percentage with grade III angiopathy in the group with normoalbuminuria compared with microalbuminuria and proteinuria (12.5 %, 40.0 % and 53.8 %, respectively); in women - a higher (\(p=0.086\) and \(p<0.01\)) percentage with grade III angiopathy in the group with proteinuria compared with normoalbuminuria and microalbuminuria (62.5 %, 29.0 % and 13.0 %, respectively) (see Fig. 1).

Significant or sex differences in the percentage of patients with retinopathy among patients with normoalbuminuria, microalbuminuria or proteinuria have not been established (Fig. 2).

When comparing the frequency of absence or presence of retinopathy between men or women with different levels of albumin in the urine, it was found (see Fig. 2): in men - a higher (\(p<0.001\), \(p=0.092\)) percentage with absence of retinopathy in the group with normoalbuminuria compared with microalbuminuria and proteinuria (70.0 %, 20.0 % and 0 %, respectively); lower (\(p=0.05\) and \(p=0.066\)) percentage with I degree retinopathy in the group with proteinuria compared with microalbuminuria and normoalbuminuria (0 %, 36.0 % and 22.5 %, respectively); higher (\(p<0.001\)) percentage with grade II retinopathy in the group with proteinuria compared with normoalbuminuria and microalbuminuria (100 %, 0 % and 4.0 %, respectively); higher (\(p<0.01\) and \(p<0.05\)) percentage with grade III retinopathy in the group with microalbuminuria compared with normoalbuminuria and proteinuria (40.0 %, 7.5 % and 0 %, respectively); in women - a higher (\(p<0.05\)) percentage with no retinopathy in the group with normoalbuminuria compared with proteinuria (54.8 % and 12.5 %, respectively); lower (\(p=0.087\) and \(p=0.070\)) percentage with
first-degree retinopathy in the group with proteinuria compared with microalbuminuria and normoalbuminuria; higher (p<0.001) percentage with grade II degree retinopathy in the group with microalbuminuria compared with normoalbuminuria and proteinuria (92.0 %, 65.0 % and 0 %, respectively), and higher (p<0.001) percentage of II degree retinopathy in the group with normoalbuminuria compared with proteinuria; higher (p<0.001) percentage with grade III degree retinopathy in the group with proteinuria compared with normoalbuminuria and microalbuminuria (92.3 %, 0 % and 0 %, respectively); in women - a higher (p=0.079) percentage with absence of neuropathy in the group with normoalbuminuria compared with microalbuminuria (12.9 % and 0 %, respectively); higher (p=0.073 and p<0.001) percentage with II degree neuropathy in the group with microalbuminuria compared with normoalbuminuria and proteinuria (91.3 %, 71.0 % and 12.5 %, respectively), and higher (p<0.001) percentage of II degree neuropathy in the group with normoalbuminuria compared with proteinuria; a higher (p<0.001) percentage with grade III neuropathy in the group with proteinuria compared with normoalbuminuria and microalbuminuria (75.0 %, 0 %, and 0 %, respectively) (see Fig. 3).

Fig. 3. Percentage of patients with T1D with neuropathy depending on the level of albumin in the urine (%). 1 - sick men with normoalbuminuria; 2 - sick women with normoalbuminuria; 3 - sick men with microalbuminuria; 4 - sick women with microalbuminuria; 5 - sick men with proteinuria; 6 - sick women with proteinuria; Row 1 - no neuropathy; Row 2 - neuropathy of the I degree; Row 3 - neuropathy of the II degree; Row 4 - neuropathy of the III degree.

Fig. 4. Systolic blood pressure in men and women with T1D depending on the level of albumin in the urine (mm Hg). Here and in the following figures, 1 - healthy men; 2 - sick men with normoalbuminuria; 3 - sick men with microalbuminuria; 4 - sick men with proteinuria; 5 - healthy women; 6 - sick women with normoalbuminuria; 7 - sick women with microalbuminuria; 8 - sick women with proteinuria; Mean - average value; Mean±SE - average value ± mean error; Mean±SD - mean value ± standard deviation.

Fig. 5. Diastolic blood pressure in men and women with T1D depending on the level of albumin in the urine (mm Hg).

Fig. 6. Pulse in men and women with T1D depending on the level of albumin in the urine (beats per minute).
The value of systolic blood pressure in healthy men was lower (p<0.05-0.01) in comparison with sick men with normo-, microalbuminuria and proteinuria. In sick men with normoalbuminuria, this indicator is lower (p<0.05-0.01) compared with men with microalbuminuria and proteinuria. Healthy women had lower (p=0.078, p<0.01) heart rate values compared to sick women with normo-, microalbuminuria and proteinuria. Patients with normoalbuminuria had lower (p<0.05-0.01) heart rate values compared with patients with microalbuminuria and proteinuria. In addition, this indicator is higher in women with proteinuria (p<0.05) compared with women with microalbuminuria (Fig. 6). Among the sexual differences of the pulse, higher (p<0.01) values of this indicator were found only in women with proteinuria (see Fig. 6).

Growth values were found higher (p<0.001) in healthy men compared to sick men with normo-, microalbuminuria and proteinuria. In patients' men with normoalbuminuria, this indicator is higher (p<0.01-0.001) compared with men with microalbuminuria and proteinuria. Healthy women had higher (p<0.05) growth values compared to sick women with normo-, microalbuminuria and proteinuria (Fig. 7). In men of all studied groups, higher (p<0.05-0.001) values of growth were found in comparison with women of similar comparison groups (see Fig. 7).

Higher (p<0.05-0.001) weight values were found in healthy men compared to sick men with normo-, microalbuminuria and proteinuria. In patients' men with normoalbuminuria, this indicator is higher (p<0.01-0.01) compared with men with microalbuminuria and proteinuria (Fig. 8). In healthy men, as well as in sick men with normoalbuminuria and proteinuria, higher (p<0.001, p=0.070) weight values were found in comparison with women of similar comparison groups (see Fig. 8).

The value of body surface area in healthy men was higher (p<0.01) value of waist girth was found in healthy men compared to sick men with microalbuminuria. In patients' men with normoalbuminuria, this indicator is higher (p<0.05-0.001) compared with men with microalbuminuria and proteinuria. In healthy women, the value of body surface area was lower (p<0.05-0.001) compared with sick women with normo-, microalbuminuria (Fig. 9). In men of all studied groups, higher (p<0.05-0.001) values of body surface area were found in comparison with women of similar comparison groups (see Fig. 9).

A higher (p<0.01) value of waist girth was found in healthy men compared to sick men with microalbuminuria. In patients' men with normoalbuminuria, this indicator is higher (p<0.05-0.001) compared with men with
microalbuminuria and proteinuria. In healthy women, the value of waist girth was lower (p<0.05-0.01, p=0.072) compared to sick women with normo-, microalbuminuria and proteinuria (Fig. 10). In men of all studied groups, higher (p<0.05-0.001, p=0.056-0.060) values of waist circumference were found in comparison with women of similar comparison groups (see Fig. 10).

Higher (p<0.05) values of body mass index in healthy men compared with sick men with proteinuria have been established. In patients' men with normoalbuminuria, this indicator is higher (p=0.086-0.097) compared with men with proteinuria and microalbuminuria. In healthy women, less (p=0.064, p<0.05) values of body mass index were found in comparison with sick women with normo- and microalbuminuria (Fig. 11). Only healthy men had higher (p<0.001) body mass index values compared to women of the same comparison group (see Fig. 11).

Discussion

To date, there are a number of studies in the literature that show that an increase in the level of albumin in the urine of people with T1D refers them to a high risk of complications from the nervous and cardiovascular systems [10, 13, 26]. For example, the definition of microalbuminuria has been proposed for use in the stratification of risk in hypertension, which is reflected in the international guidelines for hypertension [24].

There is a clear relationship between the degree of glycemic compensation and the severity of T1D complications such as angio-, retino- and neuropathy [4, 25]. According to our study, it was found that with increasing levels of albumin in the urine in most cases increases the percentage of patients with a correspondingly severe degree of these complications (angiopathy of the 3rd degree in men with normoalbuminuria - 12.5 %, with microalbuminuria - 40.0 %, with proteinuria - 53.8 %; angiopathy of the 3rd degree in women with normoalbuminuria - 29.0 %, with microalbuminuria - 13.0 %, with proteinuria - 62.5 %; retinopathy of the II-III degree in men with normoalbuminuria - 0 % and 7.5 %, with microalbuminuria - 4.0 % and 40.0 %, with proteinuria - 100 % and 0 %; retinopathy of the II-III degree in women with normoalbuminuria - 3.2 % and 9.7 %, with microalbuminuria - 4.3 % and 26.1 %, with proteinuria - 87.5 % and 0 %; neuropathy of the II-III degree in men with normoalbuminuria - 65.0 % and 0 %, with microalbuminuria - 92.0 % and 0 %, with proteinuria - 0 % and 92.3 %; neuropathy of the II-III degree in women with normoalbuminuria - 71.0 % and 0 %, with microalbuminuria - 91.3 % and 0 %, with proteinuria - 12.5 % and 75.0 %).

In patients with T1D, the development of hypertension, mainly due to the progression of diabetic nephropathy, is secondary. Secondary renal hypertension in T1D is caused by increased activity of the tissue renin-angiotensin system. The increase in systolic and diastolic pressure in this category of patients is observed in 10-15 years after the onset of the disease and converges with the diagnosis of diabetic nephropathy. In addition, aggravated heredity of hypertension plays a role in the development of diabetic nephropathy and hypertension in patients with T1D. Thus, some patients already have a predisposition to increase systolic and diastolic blood pressure, which significantly increases the risk of diabetic nephropathy. This is evidenced by the fact that among the parents of patients with T1D was recorded a higher prevalence of hypertension.
than in the general population [1, 17].

In our study in patients with normo-, microalbuminuria and proteinuria, the value of systolic and diastolic blood pressure was, in most cases, significantly higher than in healthy subjects (respectively in men by 6.1-18.3 % and 3.6-20.3 %, in women - 5.0-20.0 % and 9.1-22.8 %) and increased with increasing levels of albumin in the urine (respectively in men by 11.4 % and 16.1 %, in women - 13.3 % and 10.0 %).

Heart rhythm disorders in diabetes can occur against the background of this disease or occur due to its complications. Quite often in diabetes there is an acceleration of the pulse (tachycardia), which is due to damage to the parasympathetic nerves. Subsequently, the pathological process captures the sympathetic parts of the autonomic nervous system [2, 7]. In fact, when comparing the heart rate between healthy individuals and patients with T1D, we found its higher values in the latter (respectively, in men by 4.2-14.7 %; in women - 8.0-31.6 %). With increasing levels of albumin in the urine, the pulse tended to accelerate (respectively, in men by 10.1 %; in women - 21.8 %).

It is known that the rate of growth and development is constitutionally determined. It can be assumed that patients with diabetes have certain somatotype features. V. V. Zhmuryk and others [27], as well as Senko V. I. and others [19] found that men with T1D had short stature, short and slender upper limbs, slender and elongated lower limbs, moderately short and narrow chest, increased waist circumference and increased accumulation of fat on the lateral and anterior surfaces of the torso as a background of reduced thickness of skin and fat folds in the back. Patients women had short stature, short upper extremities, elongated lower extremities with slender thighs, wide crus in the lower third, a barrel-shaped chest, increased accumulation of fat in all areas except the shoulder and crus.

A number of studies have shown that there is a dependence of diabetes on the qualitative and quantitative indicators of body composition. Thus, females have a low mass of bone and muscle components against the background of a high mass of fat component. In men, there is a low mass of all components [6, 18, 20, 21].

Summarizing the data of studies of the anthropological status of patients with T1D, there is compliance with the results of our study. Thus, in patients with T1D subjects there were lower values of growth (respectively in men by 4.6-9.2 %; in women - 2.2-4.1 %), weight (only in men by 9.0-26.4 %) and body surface area (respectively in men by 7.2-17.7 %; in women - 4.8 % only in the group of proteinuria). The lowest values of these indicators were found in patients with proteinuria compared with patients with normo- and microalbuminuria. Body mass index in sick men, compared with healthy, was significantly lower only in the group of proteinuria (by 5.5 %); and in women - higher values in the groups of normo- and microalbuminuria (by 10.6 % and 11.2 %).

The data obtained by a number of researchers indicate that in persons with T1D in comparison with healthy subjects there is a tendency to truncal type of fat deposition, ie its transition from the extremities to the torso, which allows us to consider the topography of the latter as one of the morphological markers of T1D susceptibility [22]. In women, the presence of a truncal type of fat deposits indicates andromorphy, which is significantly higher in the group of persons with impaired carbohydrate metabolism [3]. In our study: sick women compared to healthy women had a larger waist circumference (by 5.5-11.8 %); in men with T1D - on the contrary, this figure was lower in the group of microalbuminuria (by 4.0 %).

Thus, control of general clinical and anthropometric parameters in patients with diabetic nephropathy with T1D depending on albumin in the urine allows the doctor to make optimal decisions to compensate for diabetes, reduce the risk of early and long-term complications, improve quality of life.

Conclusions

The established differences in general clinical and anthropometric parameters between patients with T1D with different levels of albumin in the urine and the degree of complications from the vascular and nervous system allow to assess the severity and compensation of the disease, and comparison of these indicators with features of the pathological process.

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