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FEATURES OF LIPID, CARBOHYDRATE METABOLISM AND RENAL FUNCTION IN PATIENTS WITH TYPE 1 DIABETES AND DIFFERENT LEVELS OF ALBUMIN IN THE URINE DEPENDING ON THE LEVEL OF CYSTATIN C

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Annotation. The aim of the study was to examine the differences in lipid, carbohydrate metabolism and renal function in patients with type 1 diabetes (T1D) with different levels of albumin in the urine depending on the level of cystatin C. The sample was 78 men and 62 women aged 22-26 years, T1D patients. The control group consisted of 8 almost healthy men and 13 almost healthy women of the same age. The level of microalbuminuria and cystatin C was determined in all patients by enzyme-linked immunosorbent assay. Biochemical evaluation of fasting glucose, fasting blood glucose, glucose 2 h after exercise, mean value of glucose, glycated hemoglobin, total cholesterol, triglycerides, GFR according to Cockcroft-Gault, CKD EPI and GFR according to cystatin C. Statistical processing of the obtained results was performed in the license package "Statistica 5.5", using non-parametric evaluation methods. In T1D patients compared to the control group found significantly higher values - fasting blood glucose, glucose 2 hours after exercise, the average value of glucose, glycated hemoglobin, total cholesterol and triglycerides, cystatin C and lower values - international normal ratio, GFR according to Cockcroft-Gault, GFR by CKD EPI and GFR by cystatin C. With increasing levels of albumin in urine in patients with cystatin C < 0.9, there were changes in the following indicators: higher values of total cholesterol in men with proteinuria compared to men with normo- and microalbuminuria; and lower values - the international normal ratio in women with microalbuminuria, compared with women with normoalbuminuria; Cockcroft-Gault GFR in men with proteinuria and GFR by CKD EPI in men with proteinuria and microalbuminuria compared to men with normoalbuminuria. With increasing levels of albumin in the urine in patients with cystatin C > 0.9 there were changes in the level of the following indicators: higher values - fasting blood glucose and triglycerides in women with proteinuria compared with women with normoalbuminuria, and glycated hemoglobin and total cholesterol compared with and microalbuminuria; international normal ratio in men with microalbuminuria, compared with men with normoalbuminuria; and smaller values - GFR level by Cockcroft-Gault in men with microalbuminuria compared to men with normoalbuminuria; GFR levels by Cockcroft-Gault in women with proteinuria compared to women with microalbuminuria and GFR levels by CKD EPI in women with proteinuria compared to women with normoalbuminuria and microalbuminuria. With increasing levels of cystatin C, a decrease in glycated hemoglobin in men and women with microalbuminuria and triglycerides in women with microalbuminuria, as well as greater values of the international normal ratio in men with normoalbuminuria and GFR on cystatin C in men and women with normoalbuminuria and micro. Thus, the study obtained results that indicate the existence of differences in the studied indicators between healthy and sick subjects, between men and women and between groups of T1D patients' men or women with different levels of albumin and cystatin C.

Keywords: type 1 diabetes, cystatin C level, urinary albumin level, biochemical parameters.

Introduction

The formation and progression of renal failure in patients with diabetes is one of the main and unresolved problems of modern health care. The progress made in recent decades in the prevention, diagnosis and treatment of kidney disease has been impressive, reducing the age-adjusted death rate from chronic renal failure (CRF) by about two-thirds in industrialized countries. However, as the most common cause of hospitalization and mortality in patients with diabetes, CRF remains an exception among these encouraging trends [13].

The development of CRF is due to the complex interaction between genetic, neurohormonal, inflammatory and biochemical changes that affect kidney function. In this regard, the growing clinical importance is given to both general biochemical parameters and preclinical early markers of diabetic nephropathy [11].

In modern diagnostics, the control of diabetes mellitus

and its compensation is carried out by measuring the level of glucose in the blood, as well as conducting a glucose tolerance test. Glycated hemoglobin is an indicator of compensation of carbohydrate metabolism during the life of erythrocytes. It allows you to detect diabetes in the early stages, which allows you to start treatment in a timely manner [1, 3].

Hyperlipidemia is one of the factors in the progression of diabetic nephropathy, because the process of formation of glomerulosclerosis and atherosclerotic plaque on the vessel wall are similar. This is explained by the structural similarity of glomerular mesangiocytes with arterial smooth muscle cells. Lipids filtered into the primary urine can affect the tubules of the renal tubules. Most patients with type 1 diabetes (T1D) have dyslipidemia: increased levels of triglycerides, total cholesterol, low-density lipoprotein and very low-density lipoprotein. At the same time, low levels of

high-density lipoproteins are detected [10].

Determination of serum cystatin C levels allows to calculate the glomerular filtration rate. It was noted that the more severe the renal pathology, the worse cystatin C is filtered in the kidneys and the higher its level in the blood. The level of cystatin C increases significantly in the early stages of renal dysfunction. Renal function may be reduced (by more than 50 %) until the level of creatinine only exceeds the upper limit of normal [4].

The levels of the above indicators are considered one of the most important biological constants that indicate the stability of the internal environment of the organism. However, there is a question of expediency of use of cystatin C as a part of multimarker panels for stratification of risk of chronic renal failure, cardiovascular catastrophes, etc.? Wouldn't multiple markers in a set display the same thing as each one? And what will be the contribution of cystatin C in such cases? Based on the results of modern scientific work, we can say that the use of multi-marker panels is based on the fact that different markers reflect the severity of different pathological processes, which in interaction cause a single pathology [7, 14, 17]. In our work, the answer to these questions will be possible in the course of comparative studies of the values of biochemical parameters in healthy and sick subjects with different levels of albumin and cystatin C.

The aim of the study was to investigate the differences in lipid, carbohydrate metabolism and renal function in T1D patients with different levels of albumin in the urine depending on the level of cystatin C.

Materials and methods

The sample consisted of 78 men and 62 women aged 22-26 years, with T1D, who underwent inpatient treatment in the therapeutic department № 1 and № 2 of the Vinnytsia Regional Highly Specialized Endocrinology Center. The control group consisted of 8 healthy men and 13 healthy women of the same age.

All patients underwent the procedure of determining the level of microalbuminuria by enzyme-linked immunosorbent assay using spectrophotometry (reagents from ORGenTec, Germany). Regulatory values of microalbumin in the set of reagents used - 0-25 µg/ml.

Venous blood samples were taken from subjects on an empty stomach in the morning (up to 9 hours) after 10-12 hours of fasting.

Blood glucose was determined by enzymatic, amperometric method on a biochemical analyzer Biosen C_Line, manufacturer EKF Diagnostic (Germany). Determination of glucose content was performed using special sensor chips. When the sample is applied to the chip sensors, β-D-glucose is converted enzymatically by glucose oxidase into gluconic acid and hydrogen peroxide, which reacts with the electrode. The measurement result was an electric current that is proportional to the glucose concentration. Reference norms of blood glucose 3.3 - 5.5

mmol/L. Blood glucose levels were determined on an empty stomach and 2 hours after a meal, and the mean was calculated.

Patients underwent glycated hemoglobin (HbA1c) testing. For this analysis, the method of high performance liquid chromatography on a D 10 analyzer, manufactured by Bio-Rad, was used. Normative values of this indicator <6 %.

International normalized ratio (INR) was determined by converting the prothrombin ratio in INR according to the table. Manual technique. Manufacturer LLC "Genesis". Reference norms up to 1.0.

Biochemical parameters such as total cholesterol and triglycerides were determined photometrically (using enzymes) on a biochemical analyzer using standard kits from Pointe Scientific (USA). Determination of total cholesterol was performed using phenol and peroxidase. The norm for this indicator is less than 5.2 mmol/L. The level of serum triglycerides was determined by the same method but with lipase and peroxidase, the norm of 0.5-1.67 mmol/L.

The level of cystatin C was determined by enzyme-linked immunosorbent assay (ELISA) using the kit RD191009100 Human Cystatin C ELISA company BioVendor (Czech Republic). Regulatory values for cystatin C are 0.57-1.12 mg/L for women and 0.6-1.11 mg/L for men.

GFR levels were calculated by creatinine (Cockcroft-Gault formula and CKD EPI) and by cystatin C. Cockcroft-Gault GFR calculation formula:

GFR (for men) = [(140 - age) x body weight] / blood creatinine] x 1.23;

GFR (for women) = [(140 - age) x body weight] / blood creatinine] x 1.05;

where, age - in years; body weight - in kg; blood creatinine - µmol/L.

The calculation of GFR by CKD-EPI was performed using an online calculator.

The formula for calculating GFR on cystatin C: GFR = 100 / cystatin C - 14.

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

Results. Discussion

A lower ($p < 0.01$ in all cases) level of fasting blood glucose was found in healthy men (4.525 ± 0.599 mmol/L) compared with sick men with normal (6.531 ± 1.950 mmol/L), microalbuminuria (7.686 ± 2.847 mmol/L). and proteinuria (8.030 ± 2.991 mmol/L), in which the level of cystatin C < 0.9 . Healthy women had lower ($p < 0.01$ in both cases) fasting blood glucose levels (4.662 ± 0.479 mmol/L) compared with sick women with normoalbuminuria (6.850 ± 1.820 mmol/L) and microalbuminuria (6.573 ± 1.648 mmol/L), in which the level of cystatin C < 0.9 .

A lower ($p < 0.001$ and $p < 0.01$) fasting blood glucose level

was found in healthy men (4.525 ± 0.599 mmol/L) compared with sick men with normo- (6.288 ± 1.229 mmol/L) and microalbuminuria (6.106 ± 1.493 mmol/L), in which the level of cystatin C > 0.9. Healthy women had lower ($p < 0.001$ in all cases) fasting blood glucose levels (4.662 ± 0.479 mmol/L) compared with sick women with normoalbuminuria (6.331 ± 1.151 mmol/L), microalbuminuria (7.342 ± 1.722 mmol/L) and proteinuria (8.771 ± 2.691 mmol/L), in which the level of cystatin C > 0.9.

Patients women with proteinuria with cystatin C > 0.9 had a higher ($p < 0.05$) fasting blood glucose level (8.771 ± 2.691 mmol/L) compared with normoalbuminuria (6.331 ± 1.151 mmol/L).

In patients men with microalbuminuria and cystatin C > 0.9, the value of this indicator was lower ($p = 0.086$) compared with women of the same comparison group (6.106 ± 1.493 mmol/L and 7.342 ± 1.722 mmol/L, respectively).

A lower ($p < 0.01$ and $p = 0.083$) blood glucose level was found 2 h after exercise in healthy men (5.175 ± 0.417 mmol/L) compared with sick men with normo- (7.319 ± 1.544 mmol/L) and microalbuminuria (7.600 ± 2.808 mmol/L), in which the level of cystatin C < 0.9 was found. Healthy women had lower ($p < 0.001$ in both cases) blood glucose levels 2 h after exercise (5.169 ± 0.471 mmol/L) compared with sick women with normoalbuminuria (7.483 ± 1.683 mmol/L) and microalbuminuria (7.791 ± 1.720 mmol/L), in which the level of cystatin C < 0.9.

A lower ($p < 0.001$ and $p < 0.05$) blood glucose level was found 2 h after exercise in healthy men (5.175 ± 0.417 mmol/L) compared with sick men with normo- (7.000 ± 1.546 mmol/L) and microalbuminuria (7.428 ± 2.195 mmol/L), in which the level of cystatin C > 0.9 was found. Healthy women had lower ($p < 0.05$ - 0.001) blood glucose levels 2 h after exercise (5.169 ± 0.471 mmol/L) compared with sick women with normoalbuminuria (7.338 ± 1.603 mmol/L), microalbuminuria (7.567 ± 2.103 mmol/L) and proteinuria (8.643 ± 4.107 mmol/L), in which the level of cystatin C > 0.9.

There was a lower ($p < 0.05$ - 0.001) average value of blood glucose in healthy men (4.850 ± 0.307 mmol/L) compared with sick men with normo- (6.569 ± 1.552 mmol/L), microalbuminuria (7.636 ± 2.601 mmol/L) and proteinuria (7.980 ± 2.682 mmol/L), in which the level of cystatin C < 0.9. In healthy women, lower ($p < 0.001$ in both cases) average blood glucose (4.915 ± 0.410 mmol/L) compared with sick women with normoalbuminuria (7.111 ± 1.351 mmol/L) and microalbuminuria (7.386 ± 1.326 mmol/L), in which the level of cystatin C < 0.9.

There was a lower ($p < 0.001$ and $p < 0.01$) average value of blood glucose in healthy men (4.850 ± 0.307 mmol/L) compared with sick men with normo- (6.635 ± 1.236 mmol/L) and microalbuminuria (6.761 ± 1.507 mmol/L), in which the level of cystatin C > 0.9. Healthy women had lower ($p < 0.001$ in all cases) average blood glucose (4.915 ± 0.410 mmol/L) compared with sick women with normoalbuminuria (6.588 ± 0.919 mmol/L), microalbuminuria (7.492 ± 1.614 mmol/L) and proteinuria (8.707 ± 3.320 mmol/L), in which

the level of cystatin C > 0.9.

A lower ($p < 0.01$ - 0.001) level of glycated hemoglobin in healthy men (4.925 ± 0.537 %) was found in comparison with sick men with normo- (9.081 ± 1.587 %), microalbuminuria (8.700 ± 1.109 %) and proteinuria (9.500 ± 1.896 %), in which the level of cystatin C < 0.9. Healthy women had lower ($p < 0.001$ in both cases) levels of glycated hemoglobin (4.823 ± 0.446 %) compared with sick women with normoalbuminuria (9.372 ± 2.014 %) and microalbuminuria (9.036 ± 1.586 %), in whom the level of cystatin C < 0.9.

A lower ($p < 0.001$ in both cases) level of glycated hemoglobin was found in healthy men (4.925 ± 0.537 %) compared with sick men with normo- (9.667 ± 2.290 %) and microalbuminuria (9.978 ± 1.993 %), in whom the level of cystatin C > 0.9. Healthy women had lower ($p < 0.001$ in all cases) levels of glycated hemoglobin (4.823 ± 0.446 %) compared with sick women with normoalbuminuria (8.792 ± 1.450 %), microalbuminuria (10.28 ± 2.04 %) and proteinuria (10.77 ± 1.39 %), in which the level of cystatin C > 0.9.

Patients women with proteinuria in whom the level of cystatin C > 0.9 had a higher ($p = 0.050$ and $p < 0.05$) level of glycated hemoglobin (10.77 ± 1.39 %) compared with patients with normoalbuminuria (8.792 ± 1.450 %) and microalbuminuria (10.28 ± 2.04 %).

In men and women with microalbuminuria, in whom the level of cystatin C < 0.9, a lower ($p = 0.069$ and $p = 0.097$) level of glycated hemoglobin was found compared with subjects of the same sex with microalbuminuria, in whom the level of cystatin C > 0.9, (respectively 8.700 ± 1.109 % and 9.978 ± 1.993 %; 9.036 ± 1.586 % and 10.28 ± 2.04 %).

A lower ($p < 0.01$) international normal ratio was found in healthy women (0.954 ± 0.066) compared to sick women with microalbuminuria (0.886 ± 0.078), in whom the level of cystatin C < 0.9.

Patients women with normoalbuminuria with cystatin C < 0.9 had a higher ($p = 0.059$) international normal ratio (0.951 ± 0.079) compared with patients with microalbuminuria (0.886 ± 0.078). Patients men with normoalbuminuria with cystatin C > 0.9 had a lower ($p = 0.053$) international normal ratio (0.908 ± 0.093) compared to patients with normoalbuminuria (0.967 ± 0.098).

Patients men with normoalbuminuria and cystatin C > 0.9 had a lower ($p = 0.063$) value of the international normal ratio compared to women of the same comparison group (0.908 ± 0.093 and 0.978 ± 0.102 , respectively).

In men with normoalbuminuria, in whom the level of cystatin C < 0.9, a higher ($p = 0.084$) international normal ratio was found compared with those of the same sex with normoalbuminuria, in whom the level of cystatin C > 0.9, (0.953 ± 0.050 and 0.908 ± 0.093 , respectively).

Healthy men had lower ($p < 0.05$) values of total cholesterol (4.813 ± 0.383 mmol/L) compared to sick men with proteinuria (5.797 ± 1.255 mmol/L), in whom the level of cystatin C < 0.9. In healthy women, lower ($p < 0.05$) values of total cholesterol (4.722 ± 0.304 mmol/L) were found

compared with sick women with normoalbuminuria (5.053 ± 0.581 mmol/L), in whom the level of cystatin C < 0.9 .

In healthy women, lower ($p < 0.05$, $p = 0.061$ and $p < 0.01$) values of total cholesterol (4.722 ± 0.304 mmol/L) compared with sick women with normoalbuminuria (5.192 ± 0.802 mmol/L), microalbuminuria (5.298 ± 1.018 mmol/L) and proteinuria (6.827 ± 1.265 mmol/L), in which the level of cystatin C > 0.9 found.

Patients women with proteinuria had higher ($p < 0.05$ in both cases) values of total cholesterol (6.827 ± 1.265 mmol/L) compared with patients with normoalbuminuria (5.192 ± 0.802 mmol/L), microalbuminuria (5.298 ± 1.018 mmol/L) in which the level of cystatin C > 0.9 .

Patients men with normoalbuminuria with cystatin C > 0.9 had lower ($p < 0.05$) total cholesterol (4.632 ± 0.766 mmol/L) compared with patients with normoalbuminuria (5.192 ± 0.802 mmol/L).

In healthy women, less ($p < 0.05$ and $p = 0.068$) values of triglycerides (1.069 ± 0.155 mmol/L) compared with sick women with microalbuminuria (1.333 ± 0.433 mmol/L) and proteinuria (2.130 ± 1.060 mmol/L), in whose cystatin level C > 0.9 .

Patients women with proteinuria had higher ($p < 0.05$) triglycerides (2.130 ± 1.060 mmol/L) compared to patients with normoalbuminuria (1.224 ± 0.535 mmol/L) with cystatin C > 0.9 .

In women with microalbuminuria, in whom the level of cystatin C < 0.9 , lower ($p = 0.061$) values of triglycerides were found in comparison with women with microalbuminuria, in whom the level of cystatin C > 0.9 , (1.000 ± 0.302 mmol/L and 1.333 ± 0.433 mmol/L).

Healthy women had lower ($p = 0.075$ and $p = 0.099$) levels of cystatin C (0.586 ± 0.072 mg/L) compared with sick women with normoalbuminuria (0.667 ± 0.150 mg/L) and microalbuminuria (0.646 ± 0.100 mg/L), in which the level of cystatin C < 0.9 .

A lower ($p < 0.001$ in both cases) level of cystatin C was found in healthy men (0.681 ± 0.117 mg/L) compared with sick men with normo- (1.277 ± 0.242 mg/L) and microalbuminuria (1.302 ± 0.262 mg/L), in which the level of cystatin C > 0.9 . Healthy women had lower ($p < 0.001$ in all cases) levels of cystatin C (0.586 ± 0.072 mg/L) compared with sick women with normoalbuminuria (1.358 ± 0.353 mg/L), microalbuminuria (1.282 ± 0.390 mg/L) and proteinuria (1.402 ± 0.662 mg/L), in which the level of cystatin C > 0.9 .

In men and women with normoalbuminuria (0.687 ± 0.159 mg/L and 0.667 ± 0.150 mg/L) and microalbuminuria (0.657 ± 0.119 mg/L and 0.646 ± 0.100 mg/L), in whom the level of cystatin C < 0.9 is lower ($p < 0.05$ in all cases) the level of cystatin C compared with subjects of the same sex with normoalbuminuria and microalbuminuria, in which the level of cystatin C > 0.9 , (1.277 ± 0.242 mg/L and 1.358 ± 0.353 mg/L and 1.302 ± 0.262 mg/L and 1.282 ± 0.390 mg/L).

A higher ($p = 0.096$) level of cystatin C was found in healthy men (0.681 ± 0.117) compared to healthy women

(0.586 ± 0.072).

A higher ($p = 0.058$, $p < 0.05$ and $p < 0.001$) level of GFR by Cockcroft-Gault in healthy men (152.4 ± 22.3 ml/min/ 1.73m^2) was found in comparison with sick men with normo- (129.4 ± 45.3 ml/min/ 1.73m^2), microalbuminuria (99.14 ± 41.22 ml/min/ 1.73m^2) and proteinuria (71.35 ± 30.46 ml/min/ 1.73m^2), in which the level of cystatin C < 0.9 .

There was a higher ($p < 0.01$ - 0.001) level of GFR by Cockcroft-Gault in healthy men (152.4 ± 22.3 ml/min/ 1.73m^2) compared with sick men with normo- (121.6 ± 27.1 ml/min/ 1.73m^2) and microalbuminuria (100.5 ± 26.2 ml/min/ 1.73m^2), in which the level of cystatin C > 0.9 . In healthy women, a higher ($p = 0.065$ and $p < 0.05$) level of GFR by Cockcroft-Gault (123.6 ± 13.4 ml/min/ 1.73m^2) was found in comparison with sick women with normoalbuminuria (122.5 ± 41.4 ml/min/ 1.73m^2) and proteinuria (71.00 ± 49.04 ml/min/ 1.73m^2), in which the level of cystatin C > 0.9 .

In patients with proteinuria, in whom the level of cystatin C < 0.9 , a lower ($p < 0.001$) level of GFR by Cockcroft-Gault (71.35 ± 30.46 ml/min/ 1.73m^2) compared with patients with normoalbuminuria (129.4 ± 45.3 ml/min/ 1.73m^2).

In patients with microalbuminuria, in whom the level of cystatin C > 0.9 , a lower ($p < 0.05$) level of GFR by Cockcroft-Gault (100.5 ± 26.2 ml/min/ 1.73m^2) compared with patients with normoalbuminuria (121.6 ± 27.1 ml/min/ 1.73m^2) found. In patients with microalbuminuria, in whom the level of cystatin C > 0.9 , a higher ($p < 0.05$) level of GFR by Cockcroft-Gault (122.0 ± 46.2 ml/min/ 1.73m^2) compared with patients with proteinuria (71.00 ± 49.04 ml/min/ 1.73m^2) found.

Healthy men had a higher ($p = 0.067$) GFR level according to Cockcroft-Gault (152.4 ± 22.3 ml/min/ 1.73m^2) compared to healthy women (123.6 ± 13.4 ml/min/ 1.73m^2).

There was a higher ($p < 0.05$ - 0.001) level of GFR by CKD EPI in healthy men (128.6 ± 6.3 mg/dl/ 0.9) compared with sick men with normo- (116.6 ± 12.6 mg/dl/ 0.9), microalbuminuria (101.4 ± 15.2 mg/dl/ 0.9) and proteinuria (87.50 ± 36.09 mg/dl/ 0.9), in which the level of cystatin C < 0.9 .

There was a higher ($p = 0.061$ and $p < 0.01$) level of GFR by CKD EPI in healthy men (128.6 ± 6.3 mg/dl/ 0.9) compared with sick men with normo- (118.8 ± 12.8 mg/dl/ 0.9) and microalbuminuria (112.2 ± 16.0 mg/dl/ 0.9), in which the level of cystatin C > 0.9 . Healthy women had a higher ($p < 0.05$) GFR level by CKD EPI (96.77 ± 26.70 mg/dl/ 0.9) compared to sick women with proteinuria (57.43 ± 45.71 mg/dl/ 0.9), in whom the level of cystatin C > 0.9 .

Patients men with normoalbuminuria with cystatin C < 0.9 had a higher ($p < 0.05$ in both cases) GFR CKD EPI (116.6 ± 12.6 mg/dl/ 0.9) compared with men with microalbuminuria (101.4 ± 15.2 mg/dl/ 0.9) and proteinuria (87.50 ± 36.09 mg/dl/ 0.9).

Patients women with proteinuria with cystatin C > 0.9 had a lower ($p < 0.05$ in both cases) GFR CKD EPI (57.43 ± 45.71 mg/dl/ 0.9) compared with patients with normoalbuminuria (100.6 ± 17.5 mg/dl/ 0.9) and microalbuminuria (101.4 ± 26.5 mg/dl/ 0.9).

In healthy men and in sick men with microalbuminuria,

in whom the level of cystatin C < 0.9, a higher ($p < 0.001$ and $p < 0.01$) level of GFR by CKD EPI (128.6 ± 6.3 ml/min/1.73m² and 118.8 ± 12.8 ml/min/1.73m²) compared with women of similar comparison groups (96.77 ± 26.70 ml/min/1.73m² and 100.6 ± 17.5 ml/min/1.73m²) found.

There was a higher ($p = 0.075$ and $p = 0.093$) level of GFR on cystatin C in healthy women (158.9 ± 20.6 ml/min/1.73m²) compared with sick women with normo- (144.6 ± 42.9 ml/min/1.73m²) and microalbuminuria (144.6 ± 25.7 ml/min/1.73m²), in which the level of cystatin C < 0.9.

A higher ($p < 0.001$ in both cases) level of GFR on cystatin C was found in healthy men (137.0 ± 27.9 ml/min/1.73m²) compared with sick men with normo- (66.85 ± 15.37 ml/min/1.73m²) and microalbuminuria (65.81 ± 16.92 ml/min/1.73m²), in which the level of cystatin C > 0.9. In healthy women, a higher ($p < 0.001$ in all cases) level of GFR on cystatin C (158.9 ± 20.6 ml/min/1.73m²) was found in comparison with sick women with normo- (64.06 ± 19.02 ml/min/1.73m²) microalbuminuria (69.33 ± 20.42 ml/min/1.73m²) and proteinuria (67.71 ± 27.87 ml/min/1.73m²), in which the level of cystatin C > 0.9.

Healthy men had a lower ($p = 0.096$) GFR level for cystatin C (137.0 ± 27.9 ml/min/1.73m²) compared with women of similar comparison groups (158.9 ± 20.6 ml/min/1.73m²).

In sick men and women with normoalbuminuria (139.7 ± 38.7 ml/min/1.73m² and 144.6 ± 42.9 ml/min/1.73m²) and microalbuminuria (141.9 ± 27.4 ml/min/1.73m² and 144.6 ± 25.7 ml/min/1.73m²), in which the level of cystatin C < 0.9, a higher ($p < 0.05$ in all cases) level of GFR for cystatin C compared with subjects of the same sex with normoalbuminuria and microalbuminuria, in which the level of cystatin C > 0.9, (66.85 ± 15.37 ml/min/1.73m² and 64.06 ± 19.02 ml/min/1.73m² and 65.81 ± 16.92 ml/min/1.73m² and 69.33 ± 20.42 ml/min/1.73m²).

An important clinical and diagnostic aspect is the assessment of the risk of progression of kidney damage. A positive correlation between serum cystatin C levels and albuminuria is shown. As a marker of GFR for cystatin C has clear advantages over creatinine, the main of which is the ability to recognize the earliest changes in this parameter [8, 15]. There is evidence that increased levels of cystatin C can detect kidney damage before microalbuminuria. Thus, in the work of M. Takir et al. (2016) an increase in serum cystatin C was found in the group of patients with decreased GFR and without microalbuminuria [16].

Simultaneously with changes in the level of cystatin C in diabetes, there are changes in the complex of biochemical parameters caused by both the pathological process itself and the resulting metabolic changes in the body. There may be an increase or decrease in the content of substances, increase or decrease in the activity of enzymes, the appearance of metabolites or abnormal forms that do not occur in a healthy person, inadequate response to the load of certain substances [5, 12].

For various pathological conditions (except genetically determined) biochemical changes are not strictly specific,

and therefore mainly take into account such criteria as "more or less", "longer-faster", "presence-absence" of organ-specific indicators, isoenzymes, etc. In fact, certain biochemical parameters are evaluated in comparison with indicators in healthy people, the degree and time of occurrence in the body, changes in the level of an indicator depending on the severity, duration of development and time of manifestation of disorders [2, 6, 9]. That is why the diagnostic sensitivity of a test is greater, the more adequate its choice and the greater the difference between the indicators in healthy and sick people. Be sure to take into account the differences between men and women, both in normal conditions and in pathology.

In our study in T1D patients, in whom the level of cystatin C < 0.9, compared with the control group found:

significantly higher values: *fasting blood glucose* in men with normo-, microalbuminuria and proteinuria - by 30.7 %, 41.1 % and 43.7 %; in women with normo-, microalbuminuria - by 31.9 % and 29.1 %; *glucose 2 h after exercise* in patients with normo- and microalbuminuria (in men - by 29.3 % and 31.9 %; in women - by 30.9 % and 33.7 %); *the average value of glucose* in patients with normo-, microalbuminuria and proteinuria - by 26.2 %, 36.5 % and 39.2 % and in women with normo-, microalbuminuria - by 30.9 % and 33.5 %; *glycated hemoglobin* in sick men with normo-, microalbuminuria and proteinuria - by 45.8 %, 43.4 % and 48.2 % and in women with normo-, microalbuminuria - by 48.5 % and 46.6 %; *total cholesterol* in sick men with proteinuria by 17.0 %; in women with normoalbuminuria - by 7.6 % and 6.6 %, respectively; *triglycerides* in sick women with microalbuminuria and proteinuria - by 19.8 %, 49.8 %; *cystatin C* in patients with normo- and microalbuminuria - by 12.1 % and 9.3 %;

and lower values: *the international normal ratio* in patients with microalbuminuria - by 7.7 %; *GFR level by Cockcroft-Gault* in sick men with normo-, microalbuminuria and proteinuria - by 17.8 %, 53.7 % and 113.6 %; *GFR levels according to CKD EPI* in patients with normo-, microalbuminuria and proteinuria - by 10.3 %, 26.8 % and 47.0 %; *GFR levels according to cystatin C* in patients with normo-, microalbuminuria - by 9.9 % and 9.9 %.

In T1D patients, in whom the level of cystatin C > 0.9, compared with the control group found:

significantly higher values: *fasting blood glucose* in men with normo- and microalbuminuria - by 28.0 % and 25.9 %; in women with normo-, microalbuminuria and proteinuria - by 26.4 %, 36.5 % and 46.9 %; *glucose 2 hours after exercise* in men with normo- and microalbuminuria - by 26.1 % and 30.3 %; in women with normo-, microalbuminuria and proteinuria - by 29.6 %, 31.7 % and 40.2 %; *the average value of glucose* in men with normo- and microalbuminuria - by 26.9 % and 28.3 %; in women with normo-, microalbuminuria and proteinuria - by 25.4 %, 34.4 % and 43.6 %; *glycated hemoglobin* in sick men with normo- and microalbuminuria - by 49.1 % and 50.6 %; in women with normo-, microalbuminuria and proteinuria - by 45.1 %, 53.1

% and 55.2 %; *total cholesterol* in sick women with normo-, microalbuminuria and proteinuria - by 9.1 %, 10.9 % and 30.8 %; *triglycerides* in sick women with microalbuminuria and proteinuria - by 19.8 %, 49.8 %; *cystatin C* in sick men with normo-, microalbuminuria - by 46.7 % and 47.7 %; in women with normo-, microalbuminuria and proteinuria - by 56.7 %, 54.3 % and 58.2 %;

and lower values: *GFR levels according to Cockcroft-Gault* in patients with normo-, microalbuminuria - by 84.8 %, 82.7 % and in women with normoalbuminuria and proteinuria - by 85.4 % and 99.2 %; *GFR levels according to CKD EPI* in men with normo-, microalbuminuria - by 8.3 %, 14.6 % and in women with proteinuria - by 68.5 %; *GFR levels for cystatin C* in men with normo-, microalbuminuria - by 104.9 %, 108.2 % and in women with normo-, microalbuminuria and proteinuria - by 148.1 %, 129.2 % and 134.7 %.

With an increase in urinary albumin levels in patients with cystatin C >0.9, there were changes in the level of the following indicators: a decrease in the level of GFR according to Cockcroft-Gault in patients with proteinuria by 44.7 %, in patients with proteinuria and microalbuminuria GRF according to CKD EPI by 15.0 % and 33.3 % compared with sick men with normoalbuminuria.

With increasing levels of albumin in the urine in patients with cystatin C >0.9 there were changes in the level of the following indicators: increase in patients women with fasting proteinuria by 38.5 %, triglycerides by 74.0 % compared with patients with normoalbuminuria; glycated hemoglobin by 22.5 % and 4.8 %, total cholesterol 33.6 % and 28.9 % compared with sick women with normoalbuminuria and microalbuminuria and a decrease in the international normal ratio in women with microalbuminuria by 7.34 % less compared with women with normoalbuminuria; GFR according to Cockcroft-Gault by 71.8 % compared with women with microalbuminuria and the level of GFR according to CKD EPI by 42.9 % and 43.4 % compared with women with normoalbuminuria and microalbuminuria.

With an increase in the level of cystatin C, a decrease in the level of glycated hemoglobin was found in men by 12.8 % and in women by 12.1 % (microalbuminuria); triglycerides in women by 25.0 % (microalbuminuria) and higher values of the international normal ratio in men by 5.0 %

(normoalbuminuria); GFR for cystatin C in men and women with normoalbuminuria and microalbuminuria by 109.0 % and 125.7 %, by 115.6 % and 108.6 %.

Sex differences of the studied indicators are established. Thus, in sick men with cystatin C >0.9 is lower: the international normal ratio by 7.2 %, total cholesterol by 10.8 % (normoalbuminuria); fasting blood glucose by 16.8 % (microalbuminuria) compared with sick women of the same comparison group. In men compared with women of similar comparison groups found: higher level of cystatin C by 62.2 %, Cockcroft-Gault GFR by 23.3 %, CKD EPI GFR by 32.9 % (control group) and lower GRF according to cystatin C by 13.8 % (control group).

Thus, a comparative study of biochemical parameters between healthy and sick subjects with different levels of albumin and cystatin C gives an idea of the functional state of the kidneys, metabolic processes in different organs and the body as a whole, which helps to clarify the nature of the pathological process, pathogenesis and prognosis disease, allows you to judge the effectiveness of treatment.

Conclusions and prospects for further development

1. Between healthy and T1D patients with varying degrees of albuminuria found differences in biochemical parameters, and they (values) are greater the higher the level of cystatin C (except INR, GFR by Cockcroft-Gault, GFR level by CKD EPI, GFR level for cystatin C).

2. Subjects with a cystatin C level <0.9 had lower values of glycated hemoglobin, triglycerides and higher values of the INR, GFR by Cockcroft-Gault and CKD EPI compared with those with a cystatin C level >0.9.

3. In T1D men compared with T1D women found higher values of cystatin C; lower values of INR, total cholesterol (normoalbuminuria) and fasting blood glucose (microalbuminuria).

In further studies it is planned to evaluate the features of lipid, carbohydrate metabolism and renal function in T1D patients depending on the stage of diabetic nephropathy and levels of GRF, which will more accurately interpret the results of research in the clinic.

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ОСОБЛИВОСТІ ПОКАЗНИКІВ ЛІПІДНОГО, ВУГЛЕВОДНОГО ОБМІНУ ТА ФУНКЦІЇ НИРОК У ХВОРИХ НА ЦУКРОВИЙ ДІАБЕТ 1 ТИПУ З РІЗНИМ РІВНЕМ АЛЬБУМІНУ В СЕЧІ ЗАЛЕЖНО ВІД РІВНЯ ЦИСТАТИНУ С

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Анотація. Мета дослідження - вивчити відмінності показників ліпідного, вуглеводного обміну та функції нирок у хворих на цукровий діабет 1 типу (ЦД 1) з різним рівнем альбуміну в сечі залежно від рівня цистатину С. Вибірка сформована з 78 чоловіків і 62 жінок віком 22-26 років, хворих на ЦД 1. Контрольна група складалась з 8 практично здорових чоловіків і 13 практично здорових жінок аналогічного віку. Усім пацієнтам імуноферментним методом визначали рівень мікроальбумінурії та цистатину С. Проводили біохімічну оцінку глюкози натще, глюкози крові натще, глюкози через 2 год. після навантаження, середнє значення глюкози, глікованого гемоглобіну, загального холестерину, тригліцеридів, міжнародного нормального відношення, ШКФ за Кокрофтом-Голтом, ШКФ за СКД EPI та ШКФ за цистатином С. Статистична обробка отриманих результатів проведена в ліцензійному пакеті "Statistica 5.5" з використанням непараметричних методів оцінки. У хворих на ЦД 1 порівняно із контрольною групою встановлено достовірно більші величини - глюкози крові натще, глюкози через 2 год. після навантаження, середнє значення глюкози, глікованого гемоглобіну, загального холестерину та тригліцеридів, цистатину С та менші величини - міжнародного нормального відношення, ШКФ за Кокрофтом-Голтом, ШКФ за СКД EPI і ШКФ за цистатином С. З наростанням рівня альбуміну в сечі у хворих із рівнем цистатину С <0,9, відмічались зміни наступних показників: більші значення - загального холестерину у чоловіків із протеїнурією порівняно з чоловіками з нормо- і мікроальбумінурією; та менші значення - міжнародного нормального відношення у жінок з мікроальбумінурією, порівняно з жінками із нормоальбумінурією; ШКФ за Кокрофтом-Голтом у чоловіків із протеїнурією та ШКФ за СКД EPI у чоловіків із протеїнурією й мікроальбумінурією порівняно з чоловіками з нормоальбумінурією. З наростанням рівня альбуміну в сечі у хворих із рівнем цистатину С >0,9 відмічалось зміни рівня наступних показників: більші значення - глюкози крові натще та тригліцеридів у жінок із протеїнурією порівняно з жінками з нормоальбумінурією, а також глікованого гемоглобіну та загального холестерину порівняно з жінками з нормоальбумінурією та мікроальбумінурією; міжнародного нормального відношення у чоловіків з мікроальбумінурією, порівняно з чоловіками із нормоальбумінурією; та менші значення - рівня ШКФ за Кокрофтом-Голтом у чоловіків із мікроальбумінурією порівняно з чоловіками з нормоальбумінурією; рівня ШКФ за Кокрофтом-Голтом у жінок із протеїнурією порівняно з жінками з мікроальбумінурією та рівня ШКФ за СКД EPI у жінок із протеїнурією порівняно з жінками з нормоальбумінурією та мікроальбумінурією. З наростанням рівня цистатину С встановлено зменшення рівня глікованого гемоглобіну у чоловіків і жінок з мікроальбумінурією та тригліцеридів у жінок з мікроальбумінурією, а також більші значення міжнародного нормального відношення у чоловіків з нормоальбумінурією та ШКФ за цистатином С у чоловіків і жінок з нормоальбумінурією і мікроальбумінурією. Таким чином, в ході дослідження отримано результати, які свідчать про існування відмінностей досліджуваних показників між здоровими та хворими досліджуваними, між чоловіками та жінками та між групами хворих на ЦД 1 чоловіків або жінок з різним рівнем альбуміну та цистатину С.

Ключові слова: цукровий діабет 1 типу, рівень цистатину С, рівень альбуміну в сечі, біохімічні показники.