SMJ Saratov Medical Journal
ISSN 2712-8253, Saratov Medical Journal
2025. Volume 6. Issue 3. Article CID e0302
DOI: 10.15275/sarmj.2025.0302

Original article Reprint

Association of cardiorenal risk predictors in patients with different phenotypes of early disorders of carbohydrate metabolism

Dilara N. Isakova[1, 2] ✉, Irina A. Troshina[1], Maria M. Butareva[2],
Valeriy V. Royuk[2], Ivan M. Petrov[1]
✉dilara-isakova@yandex.ru

[1]Tyumen State Medical University, Tyumen, Russia
[2]I.M. Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russia

Received 7 July, 2025, Accepted 29 September 2025

Abstract:
Objective: to identify associations between predictors of cardiorenal risk in patients with prediabetes and various phenotypes of early disorders of carbohydrate metabolism.
Materials and Methods. A cross-sectional cohort study was conducted on a sample of 122 patients with prediabetes in Tyumen (mean age: 46.2±8.2 years). We studied the role of predictors of cardiovascular risk and early renal damage in the development of total cardiorenal events over the course of a year. The degree of association of parameters and conditions was assessed using odds ratios.
Results. The most significant contributions to the development of concurrent early disorders of carbohydrate metabolism were made by impaired fasting glucose (IFG) and impaired glucose tolerance (IGT), which were demonstrated by the quantitative insulin sensitivity check index (QUICKI) ($p=0.036$), as well as levels of interleukin 1 beta (IL-1β) ($p=0.021$), high-sensitivity C-reactive protein (hs-CRP) ($p=0.031$), urinary cystatin C ($p=0.002$) and C-peptide ($p=0.039$). The phenotype of patients with early disorders of carbohydrate metabolism (concurrent IFG and IGT) was characterized by a 1.5-fold increase in the risk of developing concurrent cardiorenal events.
Conclusion. The combination of IFG and IGT in the group of patients with early disorders of carbohydrate metabolism demonstrates an increased risk of cardiorenal events, which requires a differentiated approach to the development of an algorithm for managing patients with different phenotypes of prediabetes.

Keywords: early disorders of carbohydrate metabolism, cardiorenal risk predictors, phenotypes of prediabetes

Cite as: Isakova DN, Troshina IA, Butareva MM, Royuk VV, Petrov IM. Association of cardiorenal risk predictors in patients with different phenotypes of early disorders of carbohydrate metabolism. *Saratov Medical Journal* 2025; 6 (3): e0302. https://doi.org/10.15275/sarmj.2025.0302

Introduction

According to the International Diabetes Federation (IDF), the number of people with diabetes mellitus (DM) will reach 578 million by 2030 [1]. The increase in the number of patients with carbohydrate metabolism disorders is associated with an increase in the prevalence of obese individuals and behavioral risk factors [2]. Moreover, early disorders of carbohydrate metabolism (EDCM) do not have specific clinical manifestations. They are characterized by few symptoms and a high incidence of late verification of the condition [3]. This emphasizes the need for proactive tactics in terms of primary prevention of EDCM, assessment of new modifiable risk factors, and optimization of the strategy for the EDCM detection. According to the ESSE-RF and ESSE-RF 2 studies, the prevalence of Type 2 DM in the Russian population among individuals 25–64 years of age is 6.9%, while the frequency of impaired fasting glucose (IFG) at the level of 6.1–7.0 mmol/L is 6.2% (with a higher prevalence in men: 7.7% vs. 5.0% in women) [4]. The EDCM is represented by two varieties: IFG and impaired glucose tolerance (IGT). According to the American Diabetes Association (ADA), prevalence of IGT in the Russian population aged 20–79 years is 2.2% [1]. Approaches to the diagnosis of EDCM are defined differently by endocrinological communities. E.g., the Russian Association of Endocrinologists defines the main criteria for diagnosing prediabetes as a fasting blood glucose level of 6.1–6.9 mmol/L, as well as glucose level two hours after ingestion of 75 g of glucose in the range of 7.8–11.1 mmol/L. According to the ADA recommendations, IFG should be diagnosed when the fasting plasma glucose level is within the range of 5.6–5.9 mmol/L. The updated recommendations of the European Society of Cardiology (ESC) demonstrate the existence of these two approaches to the diagnosis of IFG. However, specialists from ESC recommend using more stringent criteria for IFG identification: 5.6–6.9 mmol/L [5]. Regardless of diagnostic criteria, patients with EDCM also have a high risk of developing macro- and microvascular complications, such as retinopathy, nephropathy, and cardiovascular disease. Diabetic retinopathy in individuals with fasting blood glucose levels of 6.1–6.9 mmol/L or 2-hr glucose levels of 7.8–11.1 mmol/L occurred in 7.9% of cases [6]. Several studies confirmed an association between EDCM and a higher incidence of adverse cardiovascular events, as well as an increased risk of mortality from them estimated at 6–10% [7].

Objective: To identify associations between predictors of cardiorenal risk in patients with prediabetes and various phenotypes of EDCM.

Materials and methods

We conducted a cross-sectional cohort study on a sample of patients with prediabetes in Tyumen, Russia. Patients were recruited between 2020 and 2022 at the Multidisciplinary Clinic of the Tyumen State Medical University and City Polyclinic No. 4 of Tyumen. The main group of study subjects consisted of 122 patients with prediabetes, 41 to 65 years of age (mean age: 46.2±8.2 years). Inclusion criteria were as follows: fasting blood glucose levels ranging from 6.1 to 7.0 mmol/L; blood glucose levels during the oral glucose tolerance test (OGTT) between 7.8 and 11.1 mmol/L; age over 18 years; and voluntary consent to participate in the study. The exclusion criteria were Type 1 DM, Type 2 DM; exacerbation of chronic diseases; acute respiratory viral infection; functional class III or IV chronic heart failure sensu the New York Heart Association (NYHA) classification; stages 3b–5 chronic kidney disease (glomerular filtration rate [GFR] below 45 mL/min/1.73 m2); oncological diseases; moderate to severe anemia; moderate to severe liver failure; and gastrointestinal diseases.

The median values of carbohydrate metabolism parameters in the group were: fasting blood glucose – 6.31 [6.1; 6.6] mmol/L; blood glucose after 2 hrs. during OGTT – 8.2 [7.1; 9.1] mmol/L; glycated hemoglobin – 5.86 [5.6; 6.1] %. The mean value of the body mass index BMI) was 31.4±6.1 kg/m². At the time of prediabetes confirmation, IFG was detected in 40.6% of the subjects, while IGT was detected in 35.6%.

The comparison group included 44 subjects. The criterion for its establishment was a glycated hemoglobin level in the range of ≥5.7 to <6.5%, without other confirmed changes in carbohydrate metabolism parameters.

The control group included 38 apparently healthy subjects similar to the main study group by their gender and age (p>0.05).

To assess cardiorenal risk in the group of patients with EDCM, concurrent cardiorenal events (CCRE) were recorded during a year of observation. In the context of this study, the following events were considered as CCRE: episodes of new-onset angina; progression of the angina functional class; acute coronary syndrome that developed during the observation period; development of symptoms of chronic heart failure and/or an increase in the functional class of chronic heart failure (according to NYHA); development of hypertensive crisis that required calling an ambulance and/or seeking medical care in healthcare organizations twice or more; uncontrolled hypertension that required an increased dose and number of antihypertensive drugs; newly diagnosed microalbuminuria in a single urine portion of over 30 mg/mL; progression of microalbuminuria by 5 mg/mL within a year; GFR reduction by 5 mL/min/1.73 m2 or more within a year. In the group of EDCM patients, the proportion of CCRE detected during the year was 44.7% (102 patients), with a predominance in the IGT group (50.4%; 63 patients) vs. the IFG group (37.9%; 39 patients). No fatal CCRE were observed in the analyzed group during the year.

All respondents underwent anthropometric measurements with subsequent calculation of the BMI. The interpretation of the calculation results was performed according to the 1997 World Health Organization BMI-based classification of obesity. Waist circumference (WC) and hip circumference (HC) were measured in all subjects. WC in men ≥94 cm and ≥80 cm in women was regarded as a diagnostic criterion for abdominal obesity (IDF, 2005). The waist-to-hip ratio (WHR) was calculated as quotient of WC divided by HC. WHR exceeding 0.9 in men and 0.85 in women was considered an indicator of the abdominal obesity. The median and interquartile range of WC, HC and WHR in the group were 109 [93; 113] cm 114 [107; 122] cm, and 0.93 [0.87; 0.99], respectively. Gender differences were found in WC (p=0.021). Hypertension (HTN) was defined as systolic blood pressure (SBP) ≥140 mmHg and/or diastolic blood pressure (DBP) ≥90 mmHg, and/or if the patient was receiving antihypertensive therapy. HTN was detected in 73% (89/122) of the subjects, Stage 1 HTN as revealed in 43.4% (53/122) of the total sample, while 29.5% (36/122) of the total sample had Stage 2 HTN. The anxiety level was assessed using the State-Trait Anxiety Inventory (STAI) according to Spielberger et al. (1983).

Blood plasma levels of C-peptide, insulin, ghrelin, leptin, visfatin, and plasminogen activator inhibitor-1 were measured via flow fluorimetry on a dual-beam laser automated analyzer (Bio-Plex Protein Assay System, Bio-Rad, USA) using the Bio-Plex Pro Human Diabetes 10-Plex immunoassay (Bio-Rad, USA). Results were read using a Bio-Plex® 200 System automatic microplate reader (Bio-Rad, USA) and Bio-Plex Manager software (Bio-Rad, USA). The level of high-sensitivity C-reactive protein (hs-CRP) was measured by turbidimetry of latex particle agglutination using reagents from BioSystems (Spain) on a HumaLyzer device. The concentrations of IL-18 and tumor necrosis factor α (TNF-α) were measured using Interleukin-18-IFA-BEST (Russia) and Alpha-TNF-IFA-BEST (Russia). Vacuum-sealed blood collection tubes containing heparin, sodium citrate, and ethylenediaminetetraacetic acid were used (depending on the recommendations of the reagent manufacturer). When storing biological material for over 24 hours, a temperature of -70 ºC was employed to prevent the loss of hormonal and cytokine activity. We analyzed urine for microalbuminuria, while creatinine levels were assessed using a standard method with subsequent calculation of the GFR (Modification of Diet in Renal Disease). Podocin concentration, urinary and blood plasma cystatin C levels were analyzed via enzyme-linked immunosorbent assay (ELISA) using the Cystatin C-IFA-Best test system.

Insulin resistance and β-cell function were measured for all study subjects using the following formulas:

Homeostatic model assessment for insulin resistance (HOMA-IR) = glucose [mmol/L] × insulin [μU/mL] ÷ 22.5;

Quantitative insulin sensitivity check index (QUICKI) = 1 ÷ (lg (glucose [mg/dL]) + lg (insulin [μU/mL]));

HOMA1-β% (HOMA1-β) = 20 × insulin [μU/mL] ÷ (glucose [mmol/L] – 3.5).

We also measured levels of lipid profile components and carbohydrate metabolism parameters.

For biochemical parameters, we employed the following biochemical analyzers: Immunochemistry Systems and Synchron Clinical System CX 5 PRO (Beckman Coulter, USA) and HumaLyzer 3000 (HUMAN GmbH, Germany). Glycated hemoglobin was determined by turbidimetric inhibition immunoassay with the hemoglobin A1C reagent (Beckman Coulter, USA).

Our study fully complied with the ethical principles of the Declaration of Helsinki and Good Clinical Practice standard for designing, conducting, recording, and reporting clinical trials involving human subjects. The study was approved by the Ethics Committee of the Tyumen State Medical University of the Russian Federation Ministry of Healthcare. Patients were included in the study only after signing an informed consent form.

Statistical data processing was performed using SPSS Statistics 26.0 software (IBM Corp., USA). Quantitative parameters were assessed for compliance with normal distribution using the Shapiro–Wilk test or the Kolmogorov–Smirnov test. Spearman's rank correlation coefficient was used to evaluate correlations between the quantitative parameters under study. We compared groups using the nonparametric Kruskal–Wallis and Mann–Whitney tests. To analyze data in unrelated groups, presented as counts and percentages (%), the Pearson's χ^2 test or Fisher's exact test was employed. The latter was used in the case of fewer than 10 values of the expected phenomenon. When comparing more than two groups, the Benjamini–Hochberg correction procedure for multiple comparisons was applied. The strength of association between parameters and conditions was assessed using odds ratios (OR). Differences were considered statistically significant at $p < 0.05$.

Results

To differentiate patients with prediabetes within groups based on associations of clinical and metabolic parameters with different EDCM phenotypes, we identified the following groups: patients with IFG, patients with IGT, and individuals with concurrent IFG and IGT.

Analysis of the associations between clinical and metabolic parameters in IFG patients revealed statistically significant direct relationships of IFG with fat mass (p=0.05), HOMA-IR index (p=0.005), and plasma triglyceride (TG) level (p=0.05; *Table 1*). We observed a 1.3-fold increase in fasting plasma glucose level ≥6.1 mmol/L with an increase in TG concentration by 1 mmol/L (95% confidence interval [CI] 1.01-1.7), 1.1-fold increase with an increase in the HOMA-IR index value (95% CI 1.01-1.1), and 1.02-fold increase with an increase in fat mass by 1 kg (95% CI 1.01-1.05).

Anamnestic, metabolic and hormonal parameters suggested the presence of associations with the development of IGT (*Table 2*). During OGTT, the risk of increasing blood glucose values after 2 hrs. augmented with age (OR 1.1, 95% CI 1.02–1.098; p=0.002), along with the progression of insulin resistance assessed based on the HOMA-IR index (OR 1.3, 95% CI 1.05–1.6; p=0.001). The risk of developing IGT increased with increasing levels of insulin (OR 1.15, 95% CI 1.05–1.3; p=0.039) and C-peptide (OR 1.3, 95% CI 1.1–1.5; p=0.01). We observed a direct relationship between the development of IGT and leptin levels (OR 1.05, 95% CI 1.03–1.1; p=0.01).

Table 1. Prognostic significance of markers of clinical and metabolic parameters regarding the formation of the IFG phenotype of prediabetes

Parameter	Exp(β)	95% CI	p^*
Fat mass, kg	1.02	1.01–1.05	0.05
HOMA-IR	1.1	1.01–1.1	0.005
TG, mmol/L	1.3	1.01–1.7	0.05

Note: * Here and below in Tables 2 and 3: $p<0.05$; statistical significance was determined using the nonparametric Kruskal-Wallis test with Bonferroni correction for multiple comparisons. IFG, impaired fasting glucose; HOMA-IR, homeostatic model assessment for insulin resistance; TG, triglycerides.

Table 2. Prognostic value of markers of clinical and metabolic parameters regarding the formation of the IGT phenotype of prediabetes

Parameter	Exp(β)	95% CI	p^*
Anamnestic parameters			
Age, full years	1.1	1.02–1.098	0.002
Age at onset of EDCM, full years	1.05	1.02–1.09	0.006
Metabolic parameters			
HOMA-IR	1.3	1.05–1.6	0.001
TC, mmol/L	1.3	1.01–1.8	0.039
LDL, mmol/L	1.9	1.3–2.9	0.001
Hormonal parameters			
Insulin, pg/mL	1.15	1.05–1.3	0.039
C-peptide, pg/mL	1.3	1.1–1.5	0.01
Leptin, ng/mL	1.05	1.03–1.1	0.001

IGT, impaired glucose tolerance; EDCM, early disorders of carbohydrate metabolism; HOMA-IR, homeostatic model assessment for insulin resistance; TC, total cholesterol; LDL, low-density lipoproteins.

The highest contributions to the development of concurrent EDCM (IFG+IGT) were demonstrated by the QUICKI value (p=0.036), interleukin (IL)-1β levels (p=0.021), hs-CRP (p=0.031), urinary cystatin C (p=0.002), and C-peptide (p=0.039) (*Table 3*). An increase in the QUICKI value by 1 unit yielded a 3.9-fold increase in the risk of the simultaneous development of IFG and IGT (95% CI 1.1–14.3), a 2.6-fold increase in the concentration of IL-1β (95% CI 1.2–5.7), a 1.85-fold increase in the CRP-hs (95% CI 1.2–5.7), and a 1.8-fold increase in cystatin C in urine (95% CI 1.1–17.4) (*Table 3*).

Comparative analysis of parameters that demonstrated associations with various phenotypes of the EDCM is presented in the *Figure*. The IFG group of patients was characterized by lower values of the HOMA-IR (p=0.044), TNF-α (p<0.001) and lipid profile parameters, such as total cholesterol (TC; p=0.004) and low-density lipoproteins (LDL; p=0.002), vs. IGT group of patients, as well as lower levels of IL-8 (p=0.044) and IL-18 (p=0.024) vs. the subjects with concurrent IFG and IGT. During the OGTT, patients with blood glucose levels after 2 hours in the range of 7.8–11.1 mmol/L demonstrated higher values of fat mass (p=0.044), TC (p=0.014), C-peptide (p=0.003) than patients diagnosed with concurrent IFG and IGT. Also, compared with patients in the IFG group, higher values of the HOMA-IR (p=0.044), TC (p=0.004), LDL (p=0.002), and TNF-α (p<0.001) were recorded. In the group of patients with concurrent IFG and IGT, higher values of hs-CRP (p=0.044) and IL-8 (p=0.044) were revealed, as well as higher leptin levels. However, the latter did not show statistically significant differences.

Table 3. Prognostic value of markers of clinical and metabolic parameters regarding the formation of the concurrent IFG and IGT phenotypes of prediabetes

Parameter	Exp(β)	95% CI	p^*
Anamnestic and anthropometric parameters			
Age, full years	1.15	1.08–1.3	0.006
Fat mass, kg	1.05	1.01–1.1	0.045
Metabolic parameters			
HOMA-IR	1.05	1.01–1.15	0.002
HOMA-β	1.07	1.02–1.09	<0.001
QUICKI	3.9	1.1–14.3	0.036
TC, mmol/L	1.5	1.05–1.7	0.045
Hormonal parameters			
C-peptide, pg/mL	1.2	1.15–1.34	0.039
Leptin, ng/mL	1.08	1.001–1.1	0.002
Early markers of kidney damage			
Urinary cystatin C, μg/mL	1.8	1.1–17.4	0.05
Systemic low-grade inflammation markers			
hs-CRP, mg/L	1.85	1.1–3.2	0.031
TNF-α, pg/mL	1.1	1.005–1.09	0.05
IL, pg/mL:			
-1β	2.6	1.2–5.7	0.021
-6	1.2	1.01–1.4	0.036
-8	1.06	1.01–1.1	0.011
-10	1.14	1.005–1.3	0.042
-18	1.002	1.001–1.004	0.036

IFG, impaired fasting glucose; IGT, impaired glucose tolerance; HOMA-IR, homeostatic model assessment for insulin resistance; HOMA-β, homeostatic model assessment of beta-cell function; QUICKI, quantitative insulin sensitivity check index; TC, total cholesterol; hs-CRP, high-sensitivity C-reactive protein; TNF-α, tumor necrosis factor α; IL, interleukin.

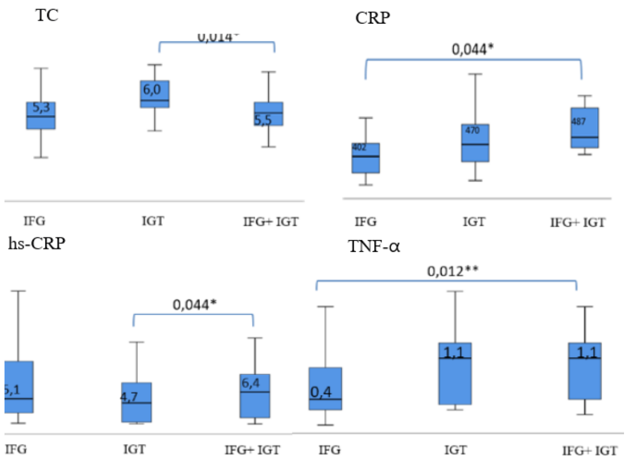

Figure. Comparative characteristics of parameters associated with the formation of prediabetes phenotypes in groups of patients with impaired fasting glycemia (IFG) and impaired glucose tolerance (IGT), and concurrent IFG and IGT. Statistical significance was determined using nonparametric criteria: *p<0.05 based on Mann–Whitney U test; **p<0.05 based on Kruskal–Wallis test with Bonferroni correction for multiple comparisons.

The most significant contributions to the development of IFG were fat mass and the associated levels of insulin resistance and dyslipidemia. IGT was associated with a later age at onset, as well as insulin resistance, dyslipidemia, and increased initial leptin levels. The concurrent IFG and IGT, in addition to the aforementioned predictors, was also associated with elevated levels of early markers of kidney damage and cardiovascular risk. However, no clear statistically significant differences were revealed when comparing the levels of these parameters in patient groups with different phenotypes of prediabetes. Hence, further research is required to accurately assess the clinical and metabolic status of each EDCM phenotype.

Taking into account the different clinical and metabolic status of patients with IFG, IGT, and concurrent IFG and IGT, the risk of vascular complications, including the likelihood of developing CCRE within a year, is different for each phenotype of EDCM (*Table 4*). When analyzing the associations of the metabolic phenotype of EDCM and the development of CCRE within a year using the Pearson's $\chi 2$ test and calculating the OR with 95% CI, statistically significant results were revealed solely for the phenotype involving concurrent IFG and IGT. The concomitant course of IFG and IGT was characterized by a 1.5-fold increase in the risk of developing vascular complications (p=0.05).

Discussion

In the management of EDCM, there is an emphasis on shifting modern hypoglycemic treatment towards managing the risks of cardiovascular and renal complications of EDCM [8]. Currently, there are discussions regarding which anthropometric, biochemical, or other parameters determine the phenotype characteristic of a high cardiovascular or cardiorenal risk [9]. Many researchers propose using the presence of metabolic dysfunction–associated steatotic liver disease (previously known as non-alcoholic fatty liver disease), visceral obesity, impaired insulin secretion, and insulin resistance as factors for improving the prognosis and prevention of Type 2 DM and cardiovascular diseases [10]. Another approach to identifying phenotypes of EDCM is the use of glycemic parameters (IFG, IGT, and concurrent IFG and IGT) [11].

Table 4. Risk assessment of developing concurrent cardiorenal events (CCRE) in groups of patients with different phenotypes of early disorders of carbohydrate metabolism

Phenotype of prediabetes	Count (%)		OR	95% CI	p
	with CCRE	without CCRE			
IFG (n=81)	38 (46.9)	43 (53.1)	0.6	0.35–1.05	0.075
IGT (n=26)	13 (50.0)	13 (50.0)	0.8	0.36–1.8	0.599
IFG+IGT (n=77)	51 (66.2)	26 (33.8)	1.5	1.1–2.6	0.05#

#p<0.05 (based on Pearson's chi-squared test).

In our study, the phenotype of patients with EDCM (concurrent IFG and IGT) was characterized by a 1.5-fold increase in the risk of developing CCRE, thereby demonstrating an unequal association of cardiovascular risk predictors with 1-year CCRE in patient groups with different phenotypes. Hyper- and hypoglycemia manifest themselves in diverse phenotypes, while detailed metabolic phenotyping with insulin resistance measurement improves the detection of patients with prediabetes and diabetic phenotypes in large population cohorts [12].

Conclusion

The concurrent IFG and IGT in a group of patients with early disorders of carbohydrate metabolism is indicative of an increased risk of cardiorenal events, which requires a differentiated approach to developing a management algorithm for patients with different phenotypes of prediabetes.

Author contributions. All authors contributed equally to the preparation of the manuscript.

Conflict of interest. The authors declare no conflicts of interest.

References

1. IDF Diabetes Atlas, 11th edition. *Brussels: International Diabetes Federation* 2025. (In Russ.)
2. Balanova YuA, Shalnova SA, Imaeva AE, at al. Prediabetes: Prevalence, associations with cardiovascular risk factors and contribution to survival in the population of the Russian Federation. *Cardiovascular Therapy and Prevention* 2024; 23(5): 4022. (In Russ.) https://www.doi.org/10.15829/1728-8800-2024-4022
3. Heianza Y, Arase Y, Fujihara K, et al. Screening for prediabetes to predict future diabetes using various cut-off points for HbA(1c) and impaired fasting glucose: the Toranomon Hospital Health Management Center Study 4 (TOPICS 4). *Diabet Med*. 2012; 29(9): e279-85. https://www.doi.org/10.1111/j.1464-5491.2012.03686.x
4. Scientific Organizing Committee of the ESSE-RF. Epidemiology of cardiovascular diseases in different regions of Russia (ESSE-RF). Rationale and design of the study. Preventive Medicine. 2013; 16(6): 25-34. (In Russ.)
5. Cosentino F, Grant PJ, Aboyans V, et al. 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD. *Eur Heart J*. 2020; 41(2): 255-323. https://www.doi.org/10.1093/eurheartj/ehz486
6. Nathan DM, Chew E, Christophi CA, et al. The prevalence of retinopathy in impaired glucose tolerance and recent-onset diabetes in the Diabetes Prevention Program. *Diabet Med*. 2007; 24(2): 137-44. https://www.doi.org/10.1111/j.1464-5491.2007.02043.x
7. Shlezinger S, Nojenshvander M, Barbaresko J, et al. Prediabetes and risk of mortality, diabetes-related complications and comorbidities: Umbrella review of meta-analyses of prospective studies. *Diabetologia* 2022; 65(2): 275-85. https://www.doi.org/10.1007/s00125-021-05592-3
8. Dedov I, Shestakova M, Mayorov A, et al. Algorithms for Specialized Medical Care for Patients with Diabetes Mellitus. 11th amendment. *Diabetes Mellitus* 2023; 26(2S): 1-157. (In Russ.) https://www.doi.org/10.14341/DM13042
9. Piller C. Dubious diagnosis. *Science* 2019; 363(6431): 1026-31. https://www.doi.org/10.1126/science.363.6431.1026
10. Stefan N. Pathogenesis and consequences in the context of prognosis and prevention of type 2 diabetes mellitus and cardiovascular disease. *Diabetes Mellitus* 2020; 23(1) :577-81. (In Russ.) https://www.doi.org/10.14341/DM10376
11. Zhou K, Yee SW, Seiser EL, et al. Variation in the glucose transporter gene SLC2A2 is associated with glycemic response to metformin. *Nat Genet*. 2016; 48(9): 1055-9. https://www.doi.org/10.1038/ng.3632
12. Abdul-Ghani MA, Matsuda M, DeFronzo RA. Strong association between insulin resistance in liver and skeletal muscle in non-diabetic subjects. *Diabet Med*. 2008; 25(11): 1289-94. https://www.doi.org/10.1111/j.1464-5491.2008.02597.x

Authors:
Dilara N. Isakova – PhD, Assistant Professor, Department of Hospital Therapy with a Course in Endocrinology; Deputy Director, Institute of Leadership and Healthcare Management, https://orcid.org/0000-0003-0898-043X;
Irina A. Troshina – DSc, Associate Professor, Chair of the Department of Hospital Therapy with a Course in Endocrinology, https://orcid.org/0000-0002-7772-8302;
Maria M. Butareva – DSc, Professor, Institute of Leadership and Healthcare Management, https://orcid.org/0000-0001-7325-2039;
Valeriy V. Royuk – PhD, Associate Professor, Director, Institute of Leadership and Healthcare Management, https://orcid.org/0000-0002-4966-3767;
Ivan M. Petrov – DSc, Associate Professor, Chancellor, https://orcid.org/0000-0001-7766-1745.