

ВНУТРЕННИЕ БОЛЕЗНИ/INTERNAL DISEASES

DOI: https://doi.org/10.60797/IRJ.2026.167.30 EDN: LHQSWO

CLINICAL AND METABOLIC PARAMETERS ACROSS DIFFERENT CLUSTERS OF DIABETES MELLITUS: A COMPARATIVE ANALYSIS

Research article

Zavalina M.A.[1,] *, Kurnikova I.A.[2], Ezhova N.F.[3], Bunjo E.[4], Maiorov V.A.[5], Ezhova A.S.[6]

[1] ORCID : 0009-0001-4010-7625;
[2] ORCID : 0000-0002-5712-9679;
[3] ORCID : 0009-0006-5948-8364;
[4] ORCID : 0009-0008-2549-1711;
[5] ORCID : 0000-0001-8227-5558;
[6] ORCID : 0009-0006-6909-465X;

[1, 2, 3, 4, 5] Patrice Lumumba Peoples' Friendship University of Russia, Moscow, Russian Federation
[3] Kutafin Moscow State Law University, Moscow, Russian Federation
[6] Pirogov Russian National Research Medical University, Moscow, Russian Federation

* Corresponding author (m.zavalina.a[at]yandex.ru)

Suggested: 29.01.2026; Accepted: 23.04.2026; Published: 18.05.2026

Abstract

In recent years, new strategies for the diagnosis and treatment of diabetes mellitus have been developed, with novel diabetes stratifications emerging from the perspective of predicting metabolic disorders and complications to facilitate a personalized treatment approach. The most noteworthy classification approach identifies five clusters, with three of them specifically encompassing patients with type 2 diabetes: Severe Insulin-Resistant Diabetes; Mild Age-Related Diabetes, Mild Obesity-Related Diabetes.

Objectives: to conduct a comparative analysis of laboratory parameters characterizing carbohydrate and lipid metabolism in patients with different diabetes phenotypes, categorized according to cluster analysis criteria.

A retrospective analysis was conducted on data from 83 patients with type 2 diabetes mellitus who were hospitalized at the endocrinology department of the Federal State Budgetary Institution "Central Clinical Hospital of Civil Aviation" between 2024 and 2025. The characteristics of the course of diabetes (age of onset, combination of complications, BMI, etc.), glycemic and lipid profile indicators, insulin, and C-peptide in patients of clusters were assessed. Severe Insulin-Resistant Diabetes (39 people), Mild Age-Related Diabetes (18 people) and Mild Obesity-Related Diabetes (26 people).

Cluster-based classification shows promise for implementing a personalized treatment approach. The study established that glycemic control was least effective in the Severe Insulin-Resistant Diabetes cluster, which also had the longest overall disease duration. Patients in the Mild Age-Related Diabetes cluster achieved diabetes compensation more frequently and demonstrated lower cardiometabolic risks. An earlier disease onset (Mild Obesity-Related Diabetes) did not consistently correlate with a more severe disease course.

Keywords: type 2 diabetes, metabolic control, clusters, cardiovascular autonomic neuropathy, diabetes complications.

ДАННЫЕ СРАВНИТЕЛЬНОГО АНАЛИЗА КЛИНИЧЕСКИХ ОСОБЕННОСТЕЙ И ПОКАЗАТЕЛЕЙ МЕТАБОЛИЧЕСКОГО КОНТРОЛЯ У ПАЦИЕНТОВ РАЗЛИЧНЫХ КЛАСТЕРОВ САХАРНОГО ДИАБЕТА

Научная статья

Завалина М.А.[1,] *, Курникова И.А.[2], Ежова Н.Ф.[3], Бунжо Э.[4], Майоров В.А.[5], Ежова А.С.[6]

[1] ORCID : 0009-0001-4010-7625;
[2] ORCID : 0000-0002-5712-9679;
[3] ORCID : 0009-0006-5948-8364;
[4] ORCID : 0009-0008-2549-1711;
[5] ORCID : 0000-0001-8227-5558;
[6] ORCID : 0009-0006-6909-465X;

[1, 2, 3, 4, 5] Российский университет дружбы народов имени Патриса Лумумбы, Москва, Российская Федерация
[3] Московский государственный юридический университет имени О.Е. Кутафина, Москва, Российская Федерация
[6] Российский национальный исследовательский медицинский университет имени Н.И. Пирогова, Москва, Российская Федерация

* Корреспондирующий автор (m.zavalina.a[at]yandex.ru)

Предложена: 29.01.2026; Принята: 23.04.2026; Опубликована: 18.05.2026

Аннотация

В последние годы формируются новые стратегии в диагностике и лечении сахарного диабета, предлагаются новые стратификации сахарного диабета с позиций прогнозирования метаболических нарушений и осложнений для формирования персонализированного подхода к лечению. Наиболее интересной представляется классификация с выделением пяти кластеров, три из которых включают пациентов с СД 2: тяжелый инсулинорезистентный диабет —

Severe Insulin-Resistant Diabetes; умеренный, связанный с ожирением — Mild Age-Related Diabetes; умеренный возрастной диабет — Mild Obesity-Related Diabetes.

Цель исследования: сравнительный анализ данных лабораторных показателей, характеризующих состояние углеводного и липидного обмена у пациентов с различными фенотипами сахарного диабета, распределенных в соответствие с критериями кластерного анализа.

Проведен ретроспективный анализ данных 83-х пациентов с сахарным диабетом 2 типа, госпитализированных в эндокринологический стационар ФГБУ «ЦКБ гражданской авиации» с 2024–2025 год. Оценивали особенности течения СД (возраст начала заболевания, совокупность осложнений, ИМТ и др.), показатели гликемического и липидного профиля, инсулин, С-пептид у пациентов из кластеров тяжелый инсулинорезистентный диабет (39 чел.), умеренный, связанный с ожирением (18 чел.) и умеренный возрастной диабет (26 чел.).

Применение кластерного распределения пациентов является перспективным направлением персонифицированной медицины, позволяющим оптимизировать терапевтические подходы и снизить частоту развития осложнений. По клиническим данным было установлено, что в кластере «тяжелый инсулинорезистентный диабет» контроль гликемии был наименее эффективным при большей общей продолжительности заболевания. У пациентов кластера «умеренный, связанный с ожирением» компенсация диабета достигалась чаще, а кардиометаболические риски были ниже. Более ранний дебют в кластере «умеренный возрастной диабет» не всегда означал более тяжелое течение.

Ключевые слова: сахарный диабет 2 типа, метаболический контроль, кластеры, кардиоваскулярная автономная нейропатия, осложнения диабета.

Introduction

Type 2 diabetes mellitus (T2DM) remains a critical public health concern in contemporary medical practice, largely because of its propensity to trigger severe complications. The steadily rising prevalence of diabetes, coupled with elevated mortality rates in affected individuals, underscores the urgent need for deeper investigation into the disease's underlying causes and pathophysiological mechanisms. Although advanced diagnostic tools and novel therapeutic and preventive strategies have been introduced, the incidence of premature disability and death among working-age diabetic patients continues to climb. A thorough analysis of current perspectives on the etiology and pathogenesis of carbohydrate metabolism dysregulation could pave the way for more efficient approaches to diagnosing, managing, and preventing complications in people with diabetes [1], [2].

In recent years, priority directions in diabetology have included both fundamental scientific research—such as studying genetic forms of diabetes, including relatively rare ones, and identifying key pathogenetic mechanisms for each—and practical aspects, which remain highly relevant. Despite all scientific advancements, diabetes remains a severe disease and is ranked among the top four pathologies leading to high population mortality. A natural prospect for further combating diabetes is the development of methods for early diagnosis and complication prevention, which requires reliable tools for prognosis assessment and risk stratification. In recent years, attempts have been made worldwide to develop new stratifications of diabetes. Therefore, it is crucial to conduct cluster analysis across different diabetes durations and in diverse cohorts to identify phenotypic groups of T2DM and validate them through cluster reproducibility. Using topological analysis based on patient-patient networks, three subgroups of T2DM have been identified. However, such classification requires patient genotype data, which is difficult to implement in real-world clinical settings. In the studies by E. Ahlqvist et al., based on key features—namely, patient age at disease onset, body mass index (BMI), GAD autoantibody testing, glycated hemoglobin (HbA1c) level, insulin resistance index (HOMA2-IR), and basal β-cell function (HOMA2-β)—five distinct groups (clusters) of diabetes have been proposed:

1. Severe Autoimmune Diabetes (SAID).
2. Severe Insulin-Deficient Diabetes (SIDD).
3. Severe Insulin-Resistant Diabetes (SIRD).
4. Mild Obesity-Related Diabetes (MOD).
5. Mild Age-Related Diabetes (MARD).

The identification and study of diabetes clusters contribute to a better assessment of the clinical course of T2DM, the risk of cardiovascular complications, and will optimize treatment and preventive measures [3].

Since insulin-independent forms of diabetes are significantly more common, and methods for a differentiated approach require further refinement, we compared the characteristics of clinical manifestations, including metabolic control parameters, specifically in patients from these groups [4].

Research methods and principles

A retrospective study examined medical records of 83 T2DM patients admitted to the Endocrinology Department of the Central Clinical Hospital of Civil Aviation from 2024 to 2025. Key parameters—including age at diabetes onset, complication profiles, BMI, glycemic and lipid markers, insulin levels, and C-peptide values—were analyzed across three clusters: SIRD (n = 39), MARD (n = 18), and MOD (n = 26)

The study was approved by the Ethics Committee of the Patrice Lumumba Peoples' Friendship University of Russia. — protocol No 8 of 14.10.2025

Main results

Normality of the distribution was assessed using the Shapiro-Wilk test. Since the data did not follow a normal distribution, subsequent calculations were based on the median [Me], and non-parametric statistical methods were used for analysis.

According to the clinical data, it was revealed that patients in the MARD group were older and had the highest age at disease onset 72,5 [63;92]. Analysis of clinical data showed that patients from this group had the worst indicators for the following parameters: arterial hypertension—18 patients (100%); chronic heart failure—3 patients (16.7%); ischemic heart

disease—7 patients (38.9%); post-infarction cardiosclerosis - 3 patients (16.7%); angiopathy of the lower extremities—17 patients (94.4%). However, patients from the MARD group had the lowest incidence of some forms of diabetic neuropathy: urogenital, gastrointestinal, cardiovascular autonomic neuropathy and peripheral neuropathy. They also had a lower body mass index compared to other patients.

The MOD group (n = 26) was characterized by the youngest age of participants 61 [38;76] and the highest body mass index—34.75 kg / m2. Participants in the MOD group had a low level of macrovascular complications. Arterial hypertension (HTN) was diagnosed in 88.5% of patients, which is a high rate, but lower than in the SIRD (97.4%) and MARD (100%) groups. The percentage of participants with chronic heart failure was 3.9%, which is the lowest rate among all the study groups. Post-infarction cardiosclerosis was detected in 3.9% of patients, which corresponds to the minimum level. Lower extremity angiopathy (LEA) was diagnosed in 84.6% of participants in the MOD group, however, these rates are lower than in the SIRD (92.3%) and MARD (94.4%) groups. Chronic kidney disease (CKD) was diagnosed in 3.9% of participants in the MOD group, indicating an extremely low rate of renal complications [5]. Despite the high frequency of lower extremity angiopathy, the prognosis in the MOD cluster is more favorable compared to the MARD cluster (due to the absence of severe macroangiopathy) and the SIRD cluster (due to a lower burden of microvascular complications) [6].

The SIRD group (n = 39) was characterized by a mean age of 68 [40;87] years and an age at diabetes onset of 51 [27;76] years. BMI = 32,3 [23,4; 47,3] kg/m² confirmed the presence of obesity, but did not reach the level observed in MOD. Patients with SIRD were found to have the most pronounced microvascular pathology: diabetic retinopathy (87.5%), CKD (71.8%), and cataracts (69.2%). Peripheral polyneuropathy was diagnosed in 100% of patients, indicating severe damage to the peripheral nervous system. The frequency of cardiac autonomic neuropathy (35.9%) was the highest among all the studied clusters, which is associated with an increased risk of cardiovascular events. Macrovascular complications are also significant: arterial hypertension (97.4%), lower extremity angiopathy (92.3%), and post-infarction cardiosclerosis (23.1%). The obtained data suggest that SIRD is the cluster with the highest risk of developing micro- and macrovascular complications (*Table 1*) [7].

Table 1 - Clinical characteristics of the compared groups

DOI: https://doi.org/10.60797/IRJ.2026.167.30.1

Criteria		SIRD	MARD	MOD
n		39	18	26
Middle age		68 [40;87]	72,5 [63;92]	61 [38;76]
Age of patients at the onset of the disease		51 [27;76]	63 [61;78]	47,5 [30;62]
BMI, kg/m2		32,3 [23,4;47,3]	29,8 [22,83;50,1]	33,26 [26,4;52]
Complications				
Diabetic retinopathy	n	35	14	20
	%	87.5	77.8	76.9
Cataract	n	27	11	14
	%	69.2	61.1	53.9
CKD	n	28	7	1
	%	71.8	38.9	3.9
Lower extremity angiopathy	n	36	17	22
	%	92.3	94.4	84.6
Coronary heart disease	n	9	7	9
	%	23.1	38.9	34.6
PICS	n	2	3	1
	%	5.1	16.7	3.9
CHF	n	3	3	1
	%	7.7	16.7	3.9
AG	n	38	18	23
	%	97.4	100	88.5
Peripheral polyneuropathy	n	39	17	26
	%	100	94.4	100
CAN	n	14	2	5
	%	35.9	11.1	19.2
DAN gastrointestinal form	n	7	0	3
	%	17.9	0	11.5
DAN urogenital form	n	6	1	2
	%	15.4	5.6	7.7

Note: BMI – body mass index, CKD – chronic kidney disease; IHD – ischemic heart disease; PICS – post-infarction cardiosclerosis; CHF – chronic heart failure; AG – arterial hypertension; CAN – cardiac autonomic neuropathy; DAN – diabetic autonomic neuropathy

The average age at which T2DM manifested differed notably across the identified clusters. The MOD cluster exhibited the youngest mean onset age, reaching 47,5 [30;62] years. This early emergence aligns with the cluster's strong link to obesity and metabolic syndrome—conditions typically arising during young adulthood and middle age.

In contrast, the SIRD cluster showed a slightly later average onset at 51 [27;76] years. The MARD cluster demonstrated the oldest mean age of T2DM onset, at 63 [61;78] years, which corroborates its association with age-dependent metabolic shifts and declining β-cell functionality.

Regarding disease duration, the SIRD cluster had the longest average span of T2DM, amounting to 17 [0;38] years. This extended duration likely contributes to more severe disturbances in carbohydrate metabolism and greater challenges in reaching glycemic control. Patients in the MARD cluster experienced a markedly shorter disease course, with an average duration of 6,5 [0;16] years. Meanwhile, individuals in the MOD cluster had an intermediate duration of 13,5 [3;27] years.

A comprehensive evaluation of the metabolic and clinical characteristics among T2DM patients underscored substantial variations across the patient clusters (*Table 2*) [8].

Thus, the postprandial glycemia level in the SIRD cluster was significantly higher (8,28 [4,09;17,7] mmol/L) than in the cluster MOD (6,35 [4,08;10,13] mmol/L). This indicates more pronounced postprandial hyperglycemia and, likely, a more severe degree of insulin resistance in patients with SIRD.

Glycemic control efficacy also differed between clusters. Target glycated hemoglobin levels (HbA1c < 7%) were achieved in 66.7% of patients in the MARD cluster, while in the SIRD and MOD clusters this figure was significantly lower—25.6% and 26.9%, respectively. These data indicate that, despite the advanced age of patients in the MARD cluster, diabetes is milder and more responsive to treatment [9].

Cardiometabolic parameters also varied across clusters. High-density lipoprotein cholesterol (HDL-C), an important marker of cardiovascular risk, was significantly higher in the MARD cluster (1,24 [0,86;2,05] mmol/L) compared with the MOD cluster (1,08 [0,72;1,62] mmol/L, $p < 0.01$). This indicates a more favorable lipid profile and a reduced risk of atherosclerotic complications in patients with age-related diabetes [10].

Table 2 - Metabolic control indicators in patients with diabetes mellitus in the compared clusters

DOI: https://doi.org/10.60797/IRJ.2026.167.30.2

Indicator		3 SIRD (39)	4 MARD (18)	5 MOD (26)	P1	P2	P3
Postprandial glycemia, mmol/L		8,28 [4,09;17,7]	7,35 [4,01;20,3]	6,35 [4,08;10,13]	0.861	0.006	0.098
Target HbA1c, %		7,5 [6,5;8]	7,5 [7;8]	7,5 [6,5;7,5]	0.481	0.001	0.043
HbA1C, %		9 [5,8;13,9]	7,15 [5,3;14,3]	8,1 [5,4;11,3]	0.013	0.009	0.718
HDL cholesterol, mmol/l		1,18 [0,71;1,63]	1,24 [0,86;2,05]	1,08 [0,72;1,62]	0.183	0.129	0.028
Onset of type 2 diabetes		51 [27;76]	63 [61;78]	47,5 [30;62]	<0.001	0.279	<0.001
Duration of the disease		17 [0;38]	6,5 [0;16]	13,5 [3;27]	<0.001	0.052	0.006
HbA1c target achieved	n	10	12	7	0.004	0.944	0.009
	%	25.6	66.7	26.9			

Note: Data is presented as M±SD, P1-reliability of the difference in clusters SIRD vs MARD, P2 -reliability of the difference in clusters SIRD vs MOD, P3 clusters reliability of the difference in clusters MARD vs MOD

Discussion

The evolution of diabetology into a mature scientific discipline has spurred the creation of innovative methodological frameworks. While a segment of the research community maintains that contemporary approaches significantly enhance our comprehension of DM, they caution against hastily discarding the established classification system, deeming such a move premature. Advocates of the novel classification contend that it offers a more nuanced representation of underlying pathogenetic pathways and facilitates tailored therapeutic decision-making.

Nevertheless, the translation of this theoretically sound and prognostically valuable classification into routine clinical workflows encounters multiple practical hurdles.

To begin with, precise categorization of patients into specific clusters necessitates a battery of laboratory assessments—notably HOMA indices—which are frequently inaccessible in many healthcare settings.

Furthermore, the demarcation lines between clusters often prove indistinct, particularly among individuals exhibiting borderline parameter values. This ambiguity underscores the urgent need for refined validation procedures and standardized diagnostic thresholds.

Lastly, the long-term efficacy of cluster-specific therapeutic strategies remains insufficiently documented. Robust evidence from large-scale randomized controlled trials is still lacking, leaving critical questions unanswered regarding the sustained benefits of personalized treatment paradigms for each cluster..

The increasing global incidence of T2DM underscores the critical need for refined patient stratification approaches [11].

Conclusion

Recent research employing cluster analysis to categorize T2DM patients has uncovered notable heterogeneity in their clinical presentations, metabolic profiles, and long-term outcomes.

Among the identified clusters, SIRD group exhibited the most aggressive disease trajectory. This subgroup was distinguished by persistently elevated post-meal blood glucose levels, suboptimal HbA1c control, the longest average duration of diabetes, and a disproportionately high incidence of both microvascular and macrovascular complications.

Conversely, individuals classified in the MARD cluster showed comparatively better glycemic management and a more advantageous lipid profile. These findings suggest a lower propensity for cardiometabolic complications in this subgroup.

Interestingly, the MOD cluster presented a unique pattern: despite an earlier onset of T2DM, these patients maintained glycemic control comparable to other clusters. This observation challenges the conventional assumption that younger age at diagnosis necessarily correlates with more severe disease progression.

These insights demonstrate that cluster-based stratification of T2DM patients holds substantial potential for advancing personalized medicine. By enabling more precise diagnosis, prognosis estimation, and therapeutic decision-making, this approach could significantly enhance clinical outcomes and mitigate complication risks in diabetes management.

Конфликт интересов

Не указан.

Рецензия

Сообщество рецензентов Международного научно-исследовательского журнала

DOI: https://doi.org/10.60797/IRJ.2026.167.30.3

Conflict of Interest

None declared.

Review

Community of Reviewers of the International Research Journal

DOI: https://doi.org/10.60797/IRJ.2026.167.30.3

Список литературы на английском языке / References in English

1. Ahlqvist E. Novel subgroups of adult-onset diabetes and their association with outcomes: a data-driven cluster analysis of six variables / E. Ahlqvist [et al.] // The Lancet Diabetes & Endocrinology. — 2018. — № 6 (5). — P. 361–369. — DOI: 10.1016/S2213-8587(18)30051-2.

2. Zou X. Novel subgroups of patients with adult-onset diabetes in Chinese and US populations / X. Zou, X. Zhou, Z. Zhu [et al.] // Lancet Diabetes Endocrinol. — 2019. — Vol. 7. — № 1. — P. 9–11. — DOI: 10.1016/S2213-8587(18)30316-4.

3. Kahkoska A.R. Validation of distinct type 2 diabetes clusters and their association with diabetes complications in the DEVOTE, LEADER and SUSTAIN-6 cardiovascular outcomes trials / A.R. Kahkoska, M.S. Geybels, K.R. Klein [et al.] // Diabetes Obes. Metab. — 2020. — Vol. 22. — № 9. — P. 1537–1547. — DOI: 10.1111/dom.14063.

4. Lim T.K. Triglyceride to HDL-cholesterol ratio and the incidence risk of type 2 diabetes in community dwelling adults: a longitudinal 12-year analysis of the Korean Genome and Epidemiology Study / T.K. Lim, H.S. Lee, Y.J. Lee // Diabetes Res. Clin. Pract. — 2020. — Vol. 163. — Article ID e108150. — DOI: 10.1016/j.diabres.2020.108150.

5. Oshima M. Sex differences in risk factors for end-stage kidney disease and death in type 2 diabetes: a retrospective cohort study / M. Oshima, Y. Iwata, T. Toyama [et al.] // J. Diabetes. — 2023. — Vol. 15. — № 3. — P. 246–254. — DOI: 10.1111/1753-0407.13367.

6. Singh S.S. Sex difference in the incidence of microvascular complications in patients with type 2 diabetes mellitus: a prospective cohort study / S.S. Singh, J.E. Roeters-van Lennep [et al.] // Acta Diabetol. — 2020. — Vol. 57. — № 6. — P. 725–732. — DOI: 10.1007/s00592-020-01489-6.

7. Kovesdy C.P. World Kidney Day Steering Committee. Obesity and kidney disease: hidden consequences of the epidemic / C.P. Kovesdy, S.L. Furth, C. Zoccali // J. Nephrol. — 2017. — Vol. 30. — № 1. — P. 1–10. — DOI: 10.1111/jorc.12194.

8. Pigeyre M. Validation of the classification for type 2 diabetes into five subgroups: a report from the ORIGIN trial / M. Pigeyre, S. Hess, M.F. Gomez [et al.] // Diabetologia. — 2022. — Vol. 65. — № 1. — P. 206–215. — DOI: 10.1007/s00125-021-05567-4.

9. Xing L. Clinical characteristics and risk of diabetic complications in data-driven clusters among type 2 diabetes / L. Xing, F. Peng, Q. Liang [et al.] // Front. Endocrinol. (Lausanne). — 2021. — Vol. 12. — Article ID 617628. — DOI: 10.3389/fendo.2021.617628.

10. Lim T.K. Triglyceride to HDL-cholesterol ratio and the incidence risk of type 2 diabetes in community dwelling adults: a longitudinal 12-year analysis of the Korean Genome and Epidemiology Study / T.K. Lim, H.S. Lee, Y.J. Lee // Diabetes Res. Clin. Pract. — 2020. — Vol. 163. — Article ID e108150. — DOI: 10.1016/j.diabres.2020.108150.

11. Dennis J.M. Precision medicine in type 2 diabetes: using individualized prediction models to optimize selection of treatment / J.M. Dennis // Diabetes. — 2020. — Vol. 69. — № 10. — P. 2075–2085. — DOI: 10.2337/dbi20-0002.