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Clinical approach to the differential diagnosis between immune-mediated diabetes and type 2 diabetes in adult patients

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A – Study Design, **B** – Data Collection, **C** – Statistical Analysis, **D** – Data Interpretation, **E** – Manuscript Preparation, **F** – Literature Search, **G** – Funds Collection

Summary **Background.** IDM/LADA is late-manifesting immune-mediated diabetes diagnosed in patients over 30 years of age. It is estimated to account for 5–10% of diabetes cases in adults.

Objectives. The aim of the study was to identify the parameters implying the diagnosis of immune-mediated diabetes among adults with new-onset diabetes.

Material and methods. Study included patients 30–50 years of age with new-onset diabetes, hospitalised between 2014 and 2019 in the Diabetology Department. Medical history, hyperglycaemia symptoms, comorbidities, anthropometric measurements and laboratory tests were analysed. The exclusion criterion was a history of pancreatitis.

Results. We analysed a group of 182 patients (mean age 38.1 ± 5.1). IDM/LADA was diagnosed in 78 (43%) patients. In the subgroup of subjects 30–35 years of age, IDM/LADA patients constituted 50.08%, whereas in the 36–50 years of age group, this constituted 38.65% of all the patients. The IDM/LADA patients were younger, had a lower body mass and BMI, noticed symptoms of diabetes before hospitalisation and more often had other autoimmune disorders. Thier C-peptide concentrations were nearly three times lower, while T2DM patients had a higher concentration of total cholesterol and triglycerides and more frequently had arterial hypertension (all $p < 0.05$). Testing for one antibody (GADA) allows one to diagnose 83% of IDM/LADA cases. Furthermore, determination of both GADA and ICA resulted in diagnosing autoimmune diabetes in 97% of all the patients.

Conclusions. With a measurement of C-peptide concentration and GADA detection, we could diagnose IDM/LADA with 89% sensitivity. Moreover, the inclusion of clinical features increased the sensitivity up to 93.5%. Considering the age criterion, there was no significant difference between the groups of patients with IDM/LADA.

Key words: C-peptide, diabetes mellitus, latent autoimmune diabetes in adults, autoantibodies.

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Background

Despite the enormous progress in developing new drugs and diagnostic methods, diabetes remains a difficult health problem. The number of people living with diabetes is still increasing, which leads to people's health deterioration and generates high economic costs for healthcare systems. Proper differentiation of the type of diabetes results in administering effective treatment that minimises the severity of complications and widespread consequences. Nowadays, WHO classifies diabetes mellitus by distinguishing six categories of the disease, i.e. type 1 diabetes (T1DM), type 2 diabetes (T2DM), hybrid forms of diabetes (with slowly evolving immune-mediated diabetes of adults which corresponds to latent diabetes in adults – LADA), other specific types, unclassified diabetes and hyperglycaemia first detected in pregnancy. Although this WHO 2019 classification is a significant improvement to the previous from 1999, researchers are still seeking a new, more refined classification due to the high heterogeneity of the condition and possible co-existence of components of different types of DM [1].

The 2019 WHO classification of diabetes moved LADA diabetes from a subtype of T1DM to a separate category of hybrid forms of diabetes, along with "ketosis-prone T2DM", and changed its name to "slowly evolving immune-mediated diabetes of adults". LADA is also not currently recognised by other associations as a formal subtype of diabetes. Nevertheless, controversy remains as to whether LADA is a discrete subtype, a milder form of T1DM, a variant of slow-developing T1DM or a mixture of T1DM and T2DM forms [2–5]. A recent consensus statement from an international panel of experts still defines LADA as a separate form of diabetes to establish diagnostic and therapeutic recommendations [6].

The first time LADA was characterised was in 1994 by Zimmet et al. [7]. This is a late-manifesting autoimmune form of diabetes, most commonly diagnosed in patients over 30 or 35 years of age, characterised by clinical insulin independence in the first months following the diagnosis, with the presence of serum antibodies against glutamic acid decarboxylase (GADA) and/or other islet antibodies – Islet Cell Cytoplasmic Autoantibodies (ICA), Insulinoma-Associated-2 Autoantibodies (IA-2), Zinc Transporter-8 Autoantibodies (ZnT8A) and a low serum peptide C level [8, 9].

This definition was later modified by Fourlanos, who specified the diagnosis criteria: age of onset < 30 years, presence of at least one antibody to β-cells and insulin independence for at least six months [10]. These criteria, being an attempt to classify LADA and an attempt to distinguish it from patients presenting the characteristics of both type 1 (genetic, immunological and metabolic traits) and type 2 (also metabolic and some clinical and anthropometric characteristics) were and are still subject to critical appraisal. Cernea et al. published an analysis of data on therapy in the group of patients with LADA. They indicate that the three basic diagnostic criteria currently suggested are not unambiguous and cannot be treated as such. According to them, the age cut-off point is an arbitrary criterion and should not rule out younger patients with a similar clinical course. The presence of antibodies, most often including GADA, seems to be the best single screening marker, although this is not specific to LADA, as Fourlanos himself emphasises in his criteria [10, 11]. The last criterion regarding the lack of need for insulin treatment within six months of diagnosis, which is most often raised when distinguishing LADA from DM1, has also been subjected to a critical analysis by these authors. They suggest that reports indicate there is a high bias in the time to insulin treatment initiation, and this does not depend on disease process but rather on the physician's clinical judgment, mostly related to presence or absence of clinical symptoms, and the presence of GADA [12]. In their analysis, Brophy et al. indicated that in centres where the routine diagnosis of newly diagnosed diabetes for the presence of anti-GAD antibodies was carried out, the initiation of insulin therapy was often based on the presence of antibodies as one of the most critical elements of the clinical decision and not on the necessity resulting from the progression of the disease.

The criterion of insulin independence in patients with features of autoimmune diabetes also requires critical evaluation concerning clinical practice. Although it would seem somehow paradoxical to initiate early insulin treatment for patients with LADA, since the disease is defined by the lack of insulin requirement at the onset of illness, and the aim of treatment would be the alteration of the risk of progression toward insulin dependency, the rationale of early insulin treatment seems logical.

The available clinical data indicates that patients with LADA who have achieved strict metabolic control through an earlier decision to initiate insulin therapy do not present a rapid decrease in β-cell function [13]. In the study by Thunander et al., they confirmed that early initiation of insulin therapy in the group of patients with LADA leads to better metabolic control of diabetes expressed by the glycosylated haemoglobin levels during a 3-year observation [14]. Several authors suggest that the rationale for early treatment is based on the improvement of glycaemic control while protecting β-cell function by down-regulating β-cell metabolism and releasing them from hyperglycaemic stress, which might be responsible for decreased β-cell antigen expression and a subsequent reduction of the T-cell response [11, 15, 16].

Since the redefining of LADA and incorporating it into the broader definition of immune-mediated diabetes is still in process, the data from literature still uses the LADA term to describe this group of patients.

In patients with LADA, there is a higher frequency of thyroid and gastric autoimmunity, HLA-DR3 and DR4 genotype, normal weight and no tendency to ketoacidosis associated with hyperglycaemia.

Although anthropometric measurements are helpful as a first-line screening, measuring C-peptide levels and the presence of islet autoantibodies are undoubtedly necessary conditions for a confirmatory LADA diagnosis. In one of the most extensive studies, LADA patients (377 patients, 9.7% of total) did not show categorically distinct clinical features of autoantibody-negative type 2 diabetes [5]. The preceding studies revealed that adult patients with immune-mediated diabetes present an earlier onset of the disease, have a lower body mass (BMI), decreased insulin secretion, diminished C-peptide concentration and an impaired response in glucagon stimulation tests than in those with type 2 diabetes. Consequently, they are more frequently treated with insulin, despite initial insulin independence [2, 17].

Furthermore, LADA patients present with lower blood pressure and triglyceride concentration than T2DM [18, 19]. Data shows that about 17% of newly diagnosed patients over 65 years of age with BMI over 30 kg/m^2 are autoantibody-positive, indicating that a more profound diagnosis of diabetes type is needed [19]. The absence of transparent criteria and the heterogeneous manifestation of the disease lead to a misdiagnosis of LADA [2, 18, 20, 21]. Attempts to characterise LADA's genetic association (by *genome-wide association studies* – GWAS) have recently been made, although not a single unique LADA locus has been found. Some of the LADA loci are shared with type 1 and type 2 diabetes as well [22]. Undoubtedly, the differentiation of diabetes type in patients over 30 years of age requires extensive consideration.

Objectives

The aim of the study was to identify parameters suggesting the diagnosis of immune-mediated DM (IDM) or LADA among patients 30–50 years of age with newly diagnosed diabetes. We searched for specific features, such as interview and examination data and biochemical and immunological assays, that could indicate the autoimmune background of diabetes before the result of the autoantibody test was obtained. Since we were unable to assess the insulin independence as a criterion for LADA diagnosis for the study group featuring the parameters of immune-mediated diabetes or the latent diabetes of adults we used the term of IDM/LADA to describe that group.

Material and methods

This retrospective study included all patients (n = 182) 30–50 years of age with de novo diabetes, hospitalised between April 2014 and September 2019 in the Internal Medicine and Diabetology Department of the Central Teaching Hospital of the Medical University of Lodz.

We analysed the medical interviews of patients – hyperglycaemia symptoms present at the time of diagnosis (polydipsia, polyuria, weight loss), family history of diabetes, comorbidities, i.e. arterial hypertension, dyslipidaemia, autoimmune diseases (AID – autoimmune thyroid disorders, coeliac disease and leukoderma), anthropometric measurements (body mass, BMI) and laboratory tests (C-peptide concentration, lipid panel, HbA_{1c}, acid-base homeostasis parameters). We measured ICA and GADA islet autoantibody titre for all patients, whilst other autoantibodies (IA-2 and ZnT8) were investigated only when the patients were negative for the presence of GADA/ICA. We used normal laboratory values applied in the Central Teaching Hospital's laboratory (C-peptide: 0.37–1.47 nmol/L; the threshold for positivity for autoantibodies: GADA > 10 U/mL, ICA > 0 U/mL, IA-2 > 20 U/mL, ZnT8 > 15 U/mL). The presence of at least one of the islet autoantibodies above the reference range resulted in IDM diagnosis. The exclusion criteria were a history of acute recurrent pancreatitis or chronic pancreatitis. Since we were unable to assess the insulin independence as criterion for LADA diagnosis for the study group featuring the parameters of immune-mediated diabetes or the latent diabetes of adults, we used the phrase IDM/LADA to describe that group.

All the statistical analyses were performed in PQ Stat (PQStat Software, Poznań, Poland, License no. 01500256). The assumption of normality for all the data was verified with the Shapiro-Wilk test. The associations between the variables

were analysed using Chi-square, Fisher exact, T-student and Mann-Whitney U tests. *P*-values < 0.05 were considered significant. We measured the sensitivity and specificity of diagnostic strategies based on a binary classification test (true positive, true negative, false negatives, false positives). Sensitivity was a proportion of correctly identified positives, and specificity was a proportion of correctly identified negatives.

Results

We analysed a group of 182 patients with newly diagnosed diabetes, between 30–50 years of age, including 43 women (23%) and 139 men (77%), with an average body weight 83.3 ± 21.6 kg among the men and 69.2 ± 21.2 kg among the women, and a median of body mass index (BMI) 26.6 kg/m^2 (95% CI: 25.5–28.0) in males and 23.6 kg/m^2 (95% CI: 20.4–26.5) in females.

The diagnosis of diabetes type was finally verified about two or three weeks following discharge from the hospital when the results of autoantibody tests were obtained. In 71% of our patients, the primary diagnosis of immune-mediated diabetes (based on the assessment of phenotypic traits, medical history and necessary laboratory test results) was later confirmed by the significantly elevated titre of autoantibodies and/or low serum level of C-peptide. There were 9 patients (12%) with an initial diagnosis of T2DM, which was subsequently changed to IDM. In 28% of the patients who had initially been diagnosed with immune-mediated diabetes due to clinical features, the diagnosis of autoimmune-mediated diabetes was not confirmed. The remaining 10% of patients presented inconclusive clinical features during hospitalisation. They were later found to be autoantibody-positive. The results of the initial clinical assessment and further laboratory verification are shown in Figure 1.

The patients were divided into two groups: the IDM group (decreased C-peptide plasma concentration below the normal range and/or autoantibody positivity) and the T2DM group (normal C-peptide concentration and lack of autoantibodies) (Tab. 1).

C-peptide concentrations were nearly three times lower in the IDM group than in the T2DM group (0.32 ± 0.23 vs 0.90 ± 0.45 nmol/L; $p < 0.0001$).

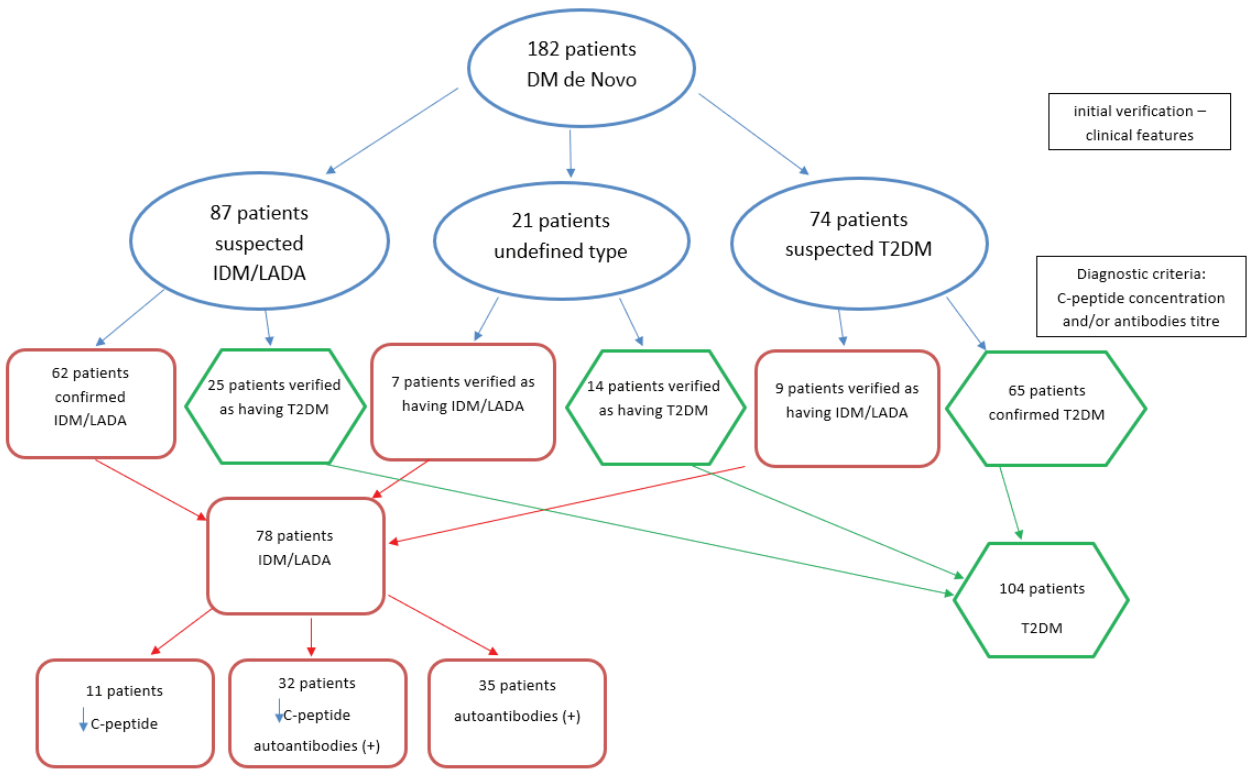

Figure 1. Results of the initial clinical assessment of diabetes type and further laboratory verification in the group of 182 patients with newly diagnosed diabetes

Table 1. Comparison of anthropometric, clinical and laboratory data between the IDM/LADA and T2DM groups

	IDM/LADA group *n* = 78	T2DM group *n* = 104	*p*
Age (years)	37.2 ± 4.9	38.7 ± 5.2	**0.040**
Height (cm)	174 ± 8	176 ± 9	0.128
Body mass (kg)	71.9 ± 17.2	94.0 ± 22.4	**< 0.0001**
BMI (kg/m^2)	23.3 (22.3–24.4)	30.0 (28.7–31.2)	**< 0.0001**
HbA_{1c} (%)	11.8 ± 2.75	11.1 ± 2.7	0.091
Blood pH	7.39 ± 0.09	7.41 ± 0.06	0.146
Base excess (mmol/L)	-3.15 ± 6.89	-1.34 ± 5.41	0.086
Total cholesterol (mmol/L)	5.36 ± 1.77	6.77 ± 4.17	**0.022**

Table 1. Comparison of anthropometric, clinical and laboratory data between the IDM/LADA and T2DM groups			
	IDM/LADA group *n* = 78	T2DM group *n* = 104	*p*
HDL cholesterol (mmol/L)	1.13 ± 0.33	1.21 ± 1.00	0.587
LDL cholesterol (mmol/L)	3.13 ± 0.88	2.99 ± 0.88	0.445
Triglycerides (mmol/L)	3.08 ± 5.08	7.75 ± 16.26	**0.047**
Ketones in urine ≥ 15 (mmol/L)	20 (25%)	19 (18%)	0.274
Symptoms of diabetes before hospitalisation	71 (91%)	80 (77%)	**0.016**
Family history of diabetes	33 (42%)	57 (55%)	0.101
HA	12 (15%)	53 (51%)	**< 0.0001**
AID	13 (17%)	2 (1.9%)	**0.0005**

Table 2. Comparison of analysed parameters between the two age groups (35 years of age and younger vs those over 35 years of age)			
	35 years of age and younger *n* = 63	Over 35 years of age *n* = 119	*p*
LADA/ T2DM	32/31	46/73	0.119
Height (cm)	176 ± 9	175 ± 8	0.255
Body mass (kg)	81.7 ± 21.9	86.0 ± 23.7	0.235
BMI (kg/m^2)	25.9 (24.4–27.5)	27.8 (26.5–29.0)	0.069
HbA_{1c} (%)	11.2 ± 2.52	11.5 ± 2.84	0.481
C-peptide concentration (nmol/L)	0.62 ± 0.48	0.64 ± 0.46	0.7827
Blood pH	7.41 ± 0.08	7.40 ± 0.08	0.490
Base excess(mmol/L)	-1.33 ± 5.88	-2.65 ± 6.38	0.242
Autoantibodies GADA/ICA/IA-2/ZnT8	23/18/-/- (including both GADA and ICA – 14)	33/26/1/1 (including both GADA and ICA – 21)	0.812
Total cholesterol (mmol/L)	5.54 ± 2.87	6.52 ± 3.70	0.134
HDL cholesterol (mmol/L)	1.08 ± 0.37	1.22 ± 0.94	0.358
LDL cholesterol (mmol/L)	2.70 ± 0.95	3.24 ± 0.78	0.0045
Triglycerides (mmol/L)	3.82 ± 4.96	6.84 ± 15.49	0.225
Ketones in urine ≥ 15 (mmol/L)	10 (16%)	29 (24%)	0.615
Symptoms of diabetes before hospitalisation	51 (81%)	100 (84%)	0.598
Family history of diabetes	33(52%)	57 (47%)	0.565
HA	18 (28%)	47 (39%)	0.143
C-peptide below normal level	15 (24%)	28 (23.5%)	0.966
AID	3 (5%)	12 (10%)	0.214
Positive for antibodies	27(42%)	40 (33%)	0.258

The patients in the IDM group were younger, had a lower body mass and BMI, more often noticed symptoms of diabetes before hospitalisation and more frequently suffered from autoimmune diseases than patients in the T2DM group. We observed elevated levels of total cholesterol and triglycerides in the T2DM group, as well as a more frequent co-occurrence of arterial hypertension.

Since, in literature, many authors apply 35 years of age as an age limitation of the LADA form of IDM, we divided all patients into two groups, i.e. those 35 years of age and younger vs individuals over 35 years of age (Tab. 2).

Apart from a higher LDL cholesterol concentration in the older group, no other relevant difference between these two cohorts was observed.

The analysis of types of autoantibodies identified in the patients is presented in Figure 2.

The most commonly detected autoantibody was GADA – positive result in 23 (72%) of the younger patients and 33 (72%) of the patients over 35 years of age. ICA was observed in 18 (28%) and 26 (22%) of the patients. One patient whose C-peptide concentration was within normal limits was IA-2 positive. Another subject whose C-peptide concentration was below the normal range was anti-ZnT8 positive. Both patients were over 35 years of age and were negative for other autoantibodies. There was no need to perform other autoantibody tests in patients 35 years of age and younger.

Considering the frequency of identified antibodies, it is worth noticing that testing for only one antibody – GADA, allows for diagnosing 83% of all IDM/LADA cases. Additionally, determination of both GADA and ICA resulted in the diagnosis of IDM/LADA diabetes in 97% of all the patients.

After analysing the diagnostic strategies adopted for distinguishing IDM/LADA type of diabetes, it may be observed that based on the measurement of C-peptide concentration and GADA detection, we could diagnose IDM/LADA with 89% sensitivity. Moreover, the inclusion of clinical features increased the sensitivity up to 93.5%.

Adopting such a diagnostic scheme did not allow for the unequivocal exclusion of patients with other forms of diabetes, including diabetes secondary to pancreatic damage due to pancreatitis. On the other hand, it did not lead to an incorrect decision to withdraw one from insulin therapy in patients who were likely to become insulin-dependent in a short time.

The sensitivity of the analysed diagnostic strategies is presented in Table 3.

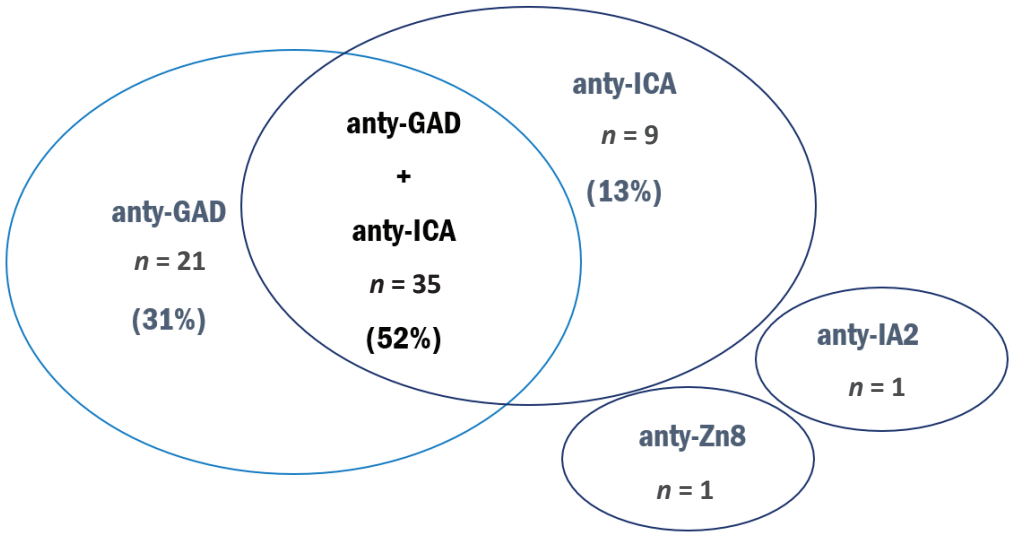

Figure 2. Prevalence of autoantibody types identified in the patients

Table 3. Sensitivity and specificity of every diagnostic pattern aimed at diagnosing IDM/LADA

Diagnostic strategy	Sensitivity	Specificity
Clinical manifestation assessment	79%	71%
Identification of GADA and ICA	83%	100%
Detection of GADA and measurement of C-peptide concentration	89%	
Assessment of clinical features, detection of GADA and measurement of C-peptide concentration	93.5%	
Identification of GADA and ICA and measurement of C-peptide concentration	98.7%	

Considering the age criterion, there was no significant difference in the analysed parameters between the groups of patients with IDM/LADA.

Discussion

Latent autoimmune diabetes in adults (LADA) combines features of both T1DM and T2DM [19] and is often defined as a hybrid form of diabetes. According to the 2020 Polish Diabetes Association's guidelines, LADA is described as a late-manifesting autoimmune form of diabetes in adults, and most commonly, it is diagnosed in patients over 35 years of age [9]. On the other hand, the American Diabetes Association does not differentiate it from immune-mediated diabetes in the Standards of Medical Care in Diabetes – 2020 [23]. In the document entitled 'Classification of diabetes mellitus 2019 [24] as a form of a hybrid type of diabetes', the World Health Organization applies the term 'slowly evolving, immune-mediated diabetes of adults'. Due to the foregoing significant discrepancies, the issue was given further consideration to verify whether LADA should be classified as a separate disease. The widely used age criterion for LADA is 30 or 35 years [25]. Our study indicates there is no significant difference among patients in the context of age; therefore, this calls into question the credibility of assigning a cut-off point for age ranges. Presumably, the above phenomenon explains the inconsistencies in the literature's age criterion [8, 9, 19]. Unfortunately, based on our observation, we cannot assess the actual distribution of diabetes types in different age groups as we only assessed the patients hospitalised in our clinic. However, there is not enough data in literature to determine the real prevalence of LADA in all patients or the population of hospitalised patients.

The detection of islet autoantibodies is still not the first-line diagnostic process in Poland due to the low accessibility of these tests and latency time. This is not common in clinical practice because of the methodology, insufficient availability in a hospital or clinic laboratory and the test's cost. For these reasons, it is usually impossible to unambiguously determine the immune-mediated background of the disease at the onset of diabetes. Therefore, we have been searching for other parameters that facilitate proper diagnosis by the time of immunological verification.

Our observation that C-peptide fasting concentration is an additional distinguishing parameter between LADA and T2DM confirms the data in literature [26–28]. Nevertheless, it should be remembered that autoimmune diabetes in adults features a diverse course of the disease, resulting in a subacute manifestation of the symptoms, lack of proneness to ketoacidosis and a detectable (for an extended period) C-peptide level (ongoing self-destruction process). Moreover, BMI is significantly lower in LADA patients. Following the stuby of G.J. Klingensmith et al. [29], we confirmed that obesity in patients does not exclude diagnosing immune-mediated diabetes. The circumstances mentioned earlier should oblige us to maintain special vigilance and order additional tests (such as C-peptide serum concentration measurement and islet autoantibody detection), even in elderly patients with the phenotype of T2DM [28].

As our study demonstrates, autoimmune comorbidity is a consecutive factor of immune-mediated diabetes mellitus [30, 31].

We could not prove the association between the type of diabetes and family history of diabetes, although this phenomenon is described in literature [20]. This observation may result from the relatively small group of patients in our study and the prevalence of T2DM in the general population. The absence of a control group and the fact that the collected data referred exclusively to hospitalised patients, who account for only a minor part of all diabetic patients, made it impossible for us to assess the significance of males' overrepresentation in the analysed population.

Our study revealed that symptoms of diabetes (e.g. hyperglycaemia), phenotypic features of T1DM, and C-peptide concentration are the most valuable factors in initial diagnosis (suspected IDM/LADA), although they do not allow for differentiation of LADA from other specific types of diabetes. To verify the diagnosis, measurement of islet autoantibodies is required, which facilitates the application of the appropriate therapy.

One of the limitations of our study was the fact that not all patients fully met the criteria proposed by Fourlanos for differ-

entiating DM1 from LADA in terms of not meeting the insulin independence criterion. This was related to the strategy of early initiation of insulin therapy in patients without absolute insulin deficiency, in line with the observations suggesting a beneficial effect of such treatment compared to treatment with insulin secretagogues [11].

This beneficial effect of early implementation of insulin treatment in autoimmune-mediated diabetes could be associated with a presumably protective effect on beta-cells in the pancreas [28]. Early insulin treatment in patients with progressive deterioration of pancreatic endocrine function but partially retained endogenous insulin excretion is associated with a lower risk of acute complications such as diabetic ketoacidosis. In these potentially safer circumstances, some patients may benefit from early gradual education in insulin therapy.

The inability to evaluate a dependence on insulin therapy in the first months following diagnosis of diabetes is an indisputable limitation of our study. This is a consequence of the study's structure – retrospective observation conducted entirely during hospitalisation, immediately after establishing the diagnosis. A further medical history of the patients was not collected in the study. Nevertheless, in literature, we can find numerous recommendations concerning the necessity of regular control of the patient in the first months following diagnosis due to the possible early ineffectiveness of oral drug therapy. In such a case, verification of the diagnosis (islet autoantibodies and fasting C-peptide concentration measurements) is required if it has not yet been done.

Moreover, it may be considered as a limitation of our study that the analysed population was only a minor part of all the patients diagnosed during that time (patients who needed hospitalisation due to hyperglycaemia < 250 mg/dl, intensified symptoms or strong suspicion of immune-mediated diabetes), and thus it should not be generalised to all patients 30–50 years of age with new-onset diabetes. A majority of patients 30–50 years of age are diagnosed in outpatient clinics and are prescribed oral drugs as first-line therapy, without earlier immunological verification of the diagnosis.

The authors of some studies point out the genetic and immunological differences between LADA and other types of immune mediated diabetes (IDM) such as T1DM [2, 27]. However, the characteristic clinical features of patients or presence of typical autoantibodies.

One of the advantages of our study is the fact that it proves that based on measurements of C-peptide concentration and one of the islet autoantibodies during hospitalisation and correlating them with clinical symptoms at the onset of diabetes, 94% of IDM/LADA cases may be appropriately diagnosed, which minimises costs and simplifies the diagnostic process.

It is worth noticing that 12% of the patients initially suspected to have T2DM were verified to be IDM/LADA, which makes us consider routine diagnostic tests for IDM in all de novo diabetes patients 30–50 years of age or more. On the other hand – for 21% of the patients initially suspected to have IDM/LADA, the initial diagnosis was verified as being T2DM, resulting in the possibility of withdrawing one from insulin treatment.

Conclusions

With a measurement of C-peptide concentration and GADA detection, we could diagnose IDM/LADA with 89% sensitivity. Moreover, the inclusion of clinical features increased the sensitivity up to 93.5%.

Considering the age criterion, there was no significant difference in the analysed parameters between the groups of patients with IDM/LADA.

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