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Znt8 antibody testing as a complementary tool in the differential diagnosis between latent autoimmune diabetes in adults (LADA) and type 2 diabetes.

Research on znt8 antibodies as a complementary tool in the differential diagnosis between latent autoimmune diabetes in adults (LADA) and type 2 diabetes mellitus

The search for Znt8 antibodies as a complementary tool in the differential diagnosis between latent autoimmune diabetes in adults (LADA) and type 2 diabetes

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ABSTRACT: Latent autoimmune diabetes in adults (LADA) is a form of diabetes mellitus characterized by the presence of autoimmunity against pancreatic beta cells, with Intermediate characteristics between type 1 diabetes mellitus (DM1) and type 2 diabetes mellitus (DM2). Due to its late onset and initial independence from insulin therapy, LADA is frequently confused with DM2, which hinders proper diagnosis and treatment. In this context, the importance of immunological markers, especially the anti-ZnT8 antibody, as a complementary tool for differential diagnosis is highlighted. This study aimed to analyze the relevance of the anti-ZnT8 antibody for the
Identification of patients with LADA. This is an integrative literature review, based on scientific articles published in national and international databases. The analyzed studies demonstrated that anti-ZnT8 contributes to the detection of pancreatic autoimmunity in individuals initially classified as having type 2 diabetes mellitus (DM2), in addition to being associated with lower functional reserve of beta cells and faster progression to insulin dependence. It is concluded that anti-ZnT8 represents a promising biomarker for improving the differential diagnosis between LADA and DM2, favoring early therapeutic interventions and a better clinical prognosis.

Keywords: LADA; ZnT8; autoantibodies; differential diagnosis; autoimmune diabetes.

ABSTRACT: Latent Autoimmune Diabetes in Adults (LADA) is a form of diabetes mellitus characterized by autoimmunity against pancreatic beta cells, presenting clinical and metabolic features intermediate between Type 1 Diabetes Mellitus (T1DM) and Type 2 Diabetes Mellitus (T2DM). Due to its late onset and initial independence from insulin therapy, LADA is often misdiagnosed as T2DM, leading to difficulties in diagnosis and appropriate treatment. In this context, immunological markers, particularly zinc transporter 8 autoantibodies (ZnT8A), have emerged as important complementary tools for differential diagnosis. This study aimed to assess the relevance of ZnT8A for identifying patients with LADA. An integrative literature review was conducted using scientific articles from national and international databases. The studies analyzed demonstrated that ZnT8A contributes to the detection of pancreatic autoimmunity in individuals initially classified as having T2DM and is associated with reduced functional beta-cell reserve and faster progression to insulin dependence. It is concluded that ZnT8A represents a promising biomarker for improving the differential diagnosis between LADA and T2DM, enabling earlier therapeutic interventions and contributing to better clinical outcomes.

Keywords: LADA; ZnT8; autoantibodies; differential diagnosis; autoimmune diabetes.

1 INTRODUCTION

Latent *autoimmune* diabetes in adults (LADA)

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Diabetes in adults is a form of autoimmune diabetes that affects adults and is characterized by...
Progressive destruction of pancreatic beta cells. Due to the initial clinical characteristics,
Many patients are diagnosed with type 2 diabetes mellitus (DM2), which makes it difficult to...
Early recognition of the disease can compromise the adoption of therapeutic strategies.
more suitable (POZZILLI; PIERALICE, 2018).

The clinical similarity between LADA and type 2 diabetes is one of the main diagnostic challenges.
challenges faced by healthcare professionals. In the early stages of the disease, patients
They often exhibit independence from insulin therapy and characteristics
Metabolic patterns consistent with type 2 diabetes. However, the presence of pancreatic autoimmunity.
promotes progressive deterioration of beta cell function, resulting in a reduction of
insulin production and the need for early insulin therapy, when compared to that of
individuals with classic type 2 diabetes (FADIGA et al., 2020; LI et al., 2020).

Given this diagnostic difficulty, immunological markers have played a role.
plays a key role in identifying autoimmune forms of diabetes. Among the biomarkers
Among those studied, the anti-ZnT8 antibody stands out as an important indicator of the response.
autoimmune disease targeting pancreatic beta cells.

Zinc transporter 8 (ZnT8), encoded by the *SLC30A8 gene,* is a protein.
transmembrane located predominantly in pancreatic beta cells and plays
plays an essential role in the intracellular transport of zinc, participating in the processes of
Storage, crystallization, and secretion of insulin. Immunological changes involving this
Proteins have been associated with pancreatic autoimmunity mechanisms observed in different forms of
autoimmune diabetes (BARRAGÁN-ÁLVAREZ et al., 2021).

The presence of anti-ZnT8 antibodies has been extensively investigated as an auxiliary tool.
in the differential diagnosis between LADA and type 2 diabetes. Studies show that this biomarker
can identify patients initially classified as having type 2 diabetes, but who
They exhibit an underlying autoimmune process consistent with LADA. Furthermore, the
Positive anti-ZnT8 results have been associated with lower functional reserve of beta cells and...
faster progression to insulin dependence, reinforcing its clinical relevance and
laboratory (FACCINETTI et al., 2016; ARAUJO et al., 2014).

Although scientific advances have broadened our knowledge of biomarkers
Immunological factors associated with LADA still present challenges to its routine use in
In clinical practice, it becomes important to understand the potential of anti-ZnT8.
as a complementary tool in the differential diagnosis between LADA and DM2, contributing

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for greater diagnostic accuracy and better therapeutic guidance. The realization of this study
This is justified by the need to deepen the understanding of the applicability of anti-ZnT8.
in the identification of latent autoimmune diabetes in adults, considering its relevance to the
Reducing diagnostic errors and enabling the implementation of more effective therapeutic strategies.
suitable for patients affected by the disease. Given this scenario, the following question arises.
Research topic: what is the contribution of the anti-ZnT8 antibody to the differential diagnosis between
What are the characteristics of Latent Autoimmune Diabetes in Adults (LADA) and Type 2 Diabetes Mellitus (DM2)?
Therefore, the aim of this article was to analyze the role of the anti-ZnT8 antibody in
differential diagnosis between Latent Autoimmune Diabetes in Adults (LADA) and Diabetes
Type 2 Diabetes Mellitus (DM2), highlighting its importance in identifying autoimmunity.
pancreatic and in improving diagnostic accuracy.

2. THEORETICAL FRAMEWORK

Latent autoimmune diabetes in adults (LADA) is a form of diabetes characterized by
Progressive destruction of pancreatic beta cells mediated by autoimmune mechanisms.
Recognized as a heterogeneous condition, this disease presents clinical characteristics and
Immunological factors differentiate it from other forms of diabetes, making its diagnosis a...
A challenge in clinical practice. The presence of circulating autoantibodies against cell antigens.
Beta beta constitutes one of the main pieces of evidence of its autoimmune nature and one of the criteria.
used for their identification (POZZILLI; PIERALICE, 2018).
The pathophysiology of LADA is directly related to the presence of autoimmune mechanisms.
which promote the progressive destruction of pancreatic beta cells. These cells are
responsible for the synthesis and secretion of insulin, a hormone fundamental for the regulation of
glucose levels in the body. When an inappropriate immune response occurs, the
The immune system begins to recognize components of beta cells as structures.
foreign substances, triggering an inflammatory process capable of compromising their function and
survival (FADIGA et al., 2020).
Cell destruction is primarily mediated by autoreactive T lymphocytes and the production of
of specific autoantibodies against proteins present in pancreatic beta cells. Although
autoantibodies are not considered the primary agents responsible for cell destruction.
Its presence constitutes important evidence of pancreatic autoimmunity and is widely known.
used for diagnostic and **prognostic** purposes (FADIGA et al., 2020; MOOSAIE et al., 2021).

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Among the most studied autoantibodies, antibodies against decarboxylase of stand out.
glutamic acid (anti-GAD), the protein tyrosine phosphatase IA-2 (IA-2A), and the transporter of
Zinc 8 (anti-ZnT8). Identifying these markers makes it possible to distinguish the forms
autoimmune forms of diabetes, as well as other non-autoimmune forms of the disease, contribute to a higher risk of autoimmune diabetes.
diagnostic accuracy (SILKO et al., 2016).

Zinc transporter 8 (ZnT8) is a transmembrane protein predominantly expressed
in pancreatic beta cells and encoded by the SLC30A8 gene. Its main function is
transport zinc ions into the interior of insulin-secreting granules, participating
directly from the storage, crystallization, and secretion processes of this hormone.
(BAUMANN et al., 2020; TRABUCCHI et al., 2012). Zinc plays an essential role
in the formation of the crystalline insulin complexes present in pancreatic granules.
Form, changes in the expression or functioning of ZnT8 can directly interfere with
glycemic homeostasis and hormonal secretion mechanisms. In addition to its importance
In physiological terms, this protein has become the target of scientific interest due to its role in
autoimmune processes associated with diabetes (BARRAGÁN-ÁLVAREZ et al., 2021).

Recent research demonstrates that ZnT8 is one of the main autoantigens involved in
autoimmune diabetes. Exposure of this antigen to the immune system can trigger it.
production of specific autoantibodies, contributing to the development and progression
from the destruction of pancreatic beta cells (FACCINETTI et al., 2016).

Anti-ZnT8 antibodies are autoantibodies directed against the zinc transporter 8 present
in pancreatic beta cells. His discovery represented an important advance in
understanding the immunological mechanisms related to autoimmune diabetes, expanding
The diagnostic possibilities for identifying the disease. The production of these autoantibodies.
This results from the loss of immunological tolerance to pancreatic cellular components. From
As a result of this process, the immune system begins to recognize ZnT8 as an antigen.
triggering a specific immune response against that protein. The presence of
Anti-ZnT8 antibodies have been observed in different forms of autoimmune diabetes.
including DM1 and LADA (Araújo et al., 2014).

Studies conducted in different populations demonstrate that anti-ZnT8 antibodies
They exhibit high specificity for autoimmune processes related to diabetes. In addition
Furthermore, their identification can complement the investigation carried out through other means.
immunological markers, increasing the diagnostic capacity of laboratory tests.
available (FACCINETTI et al., 2016). The clinical relevance of these autoantibodies is

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related not only to its ability to identify the presence of autoimmunity, but
also to its association with disease progression. Scientific evidence suggests that
Individuals who test positive for anti-ZnT8 may exhibit greater impairment of function.
pancreatic and faster progression to insulin dependence (LI et al., 2020).
The differential diagnosis between latent autoimmune diabetes in adults and type 1 diabetes mellitus.
2 constitutes one of the greatest challenges in clinical practice. The similarity between the manifestations
The initial stages of these two conditions often make early identification of the nature difficult.
LADA's autoimmune nature contributes to poor diagnostic performance, leading to misdiagnosis and inappropriate treatment approaches.
In this context, anti-ZnT8 antibodies emerge as an important tool.
complementary to laboratory investigation. The presence of these autoantibodies allows
to identify underlying autoimmune mechanisms in patients initially classified as
individuals with type 2 diabetes, contributing to a more precise differentiation between the two diseases.
(RIDNER et al., 2015).
Studies show that individuals who test positive for anti-ZnT8 frequently
They exhibit characteristics consistent with autoimmune diabetes, including reduced reserve.
Pancreatic dysfunction, more rapid decline in insulin secretion, and earlier need for insulin.
of insulin therapy. These findings reinforce the importance of immunological investigation in
patients with suspected LADA, especially those whose clinical course does not
This corresponds to the expected profile for classic type 2 diabetes (LI et al., 2020; MOOSAIE et al., 2021).
Furthermore, the use of anti-ZnT8 in combination with other immunological markers
This can significantly increase the diagnostic sensitivity for identifying LADA.
Therefore, the combined analysis of autoantibodies allows for greater accuracy in the classification of
patients, favoring individualized therapeutic interventions and contributing to a
better clinical prognosis (TRABUCCHI et al., 2012). Given the available evidence in
Scientific literature shows that the anti-ZnT8 antibody has significant potential as
A complementary biomarker in the differential diagnosis between LADA and type 2 diabetes. Its use may
to aid in the early recognition of pancreatic autoimmunity, promoting advancements
important in clinical and laboratory practice focused on the diagnosis of autoimmune diabetes.

3. MATERIALS AND METHODS

This study is characterized as a bibliographic research, of a descriptive nature and
A qualitative approach, with the aim of analyzing and interpreting existing scientific evidence.

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published on the immunological mechanisms involved in Latent Autoimmune Diabetes
Adult (LADA), with emphasis on the Zinc Transporter 8 (ZnT8) protein and its
respective autoantibodies (anti-ZnT8) as a complementary tool in diagnosis
The difference in relation to Type 2 Diabetes Mellitus (DM2). The research seeks to understand the
The role of ZnT8 in pancreatic autoimmunity, its association with beta cell destruction, and its
relevance as an immunological marker for the early identification of patients with LADA.
Data collection was carried out through a bibliographic survey in databases.
CAPES Periodicals Portal and Virtual Health Library (BVS). For the strategy of
In the search, descriptors related to the topic were used, including "LADA" and "Diabetes".
Mellitus Type 2", "ZnT8", "Anti-ZnT8 Autoantibodies", "Autoimmunity", "Diagnosis
"Differential" and "Autoimmune Diabetes", combined using the Boolean operators AND and
OR. Scientific articles published between 2016 and 2026, available in [reference to source], were selected.
The text must be complete and in Portuguese, English, and Spanish. Inclusion criteria considered were...
studies that address the immunological, clinical, and laboratory aspects of LADA,
especially those related to the ZnT8 protein, to anti-ZnT8 and anti-GAD autoantibodies
and anti-IA-2, as well as the contribution of these autoantibodies to the differential diagnosis between
LADA and DM2. Duplicate articles, incomplete studies, and simple abstracts were excluded.
publications that are not directly related to the proposed topic.
The data analysis was conducted in a qualitative and descriptive manner, through critical reading.
from the interpretation and comparison of the information obtained in the selected studies. They were
The focus was primarily on the immunological markers involved in the identification of LADA.
with an emphasis on anti-ZnT8 autoantibodies and their clinical applicability as a tool.
complementary to the diagnosis. Additionally, anti-GAD autoantibodies were evaluated and
anti-IA-2, as well as C-peptide dosage for analysis of residual beta cell function.
pancreatic characteristics were also compared.
Laboratory findings observed among patients with LADA and type 2 diabetes, aiming to highlight the importance
of ZnT8 and its autoantibodies for early diagnosis and proper classification of
illness.

4. RESULTS AND DISCUSSION

After a critical analysis of the articles available in the databases and in accordance with the criteria
Based on pre-established inclusion and exclusion criteria, 8 articles were selected that address

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The topic of this article is satisfactorily addressed. The most relevant data from these studies were... presented in the table below (Table 1).

Table 1 – Summary of articles selected from the databases

Objective Title:	Authors		Conclusion
Adult-onset autoimmune diabetes: comparative analysis of classical and latent presentation	Fatigue et al., 2020	To characterize patients with autoimmune diabetes followed at a tertiary center, comparing classic type 1 diabetes mellitus (DM1) and LADA.	Patients with LADA developed microvascular complications more frequently over the course of the disease, namely diabetic nephropathy, and presented with metabolic syndrome more frequently.
Biphasic Decline Pattern of Beta-cell Function in Adult-onset Latent Autoimmune Diabetes: an 8-year Prospective Study	Li et al., 2020	To investigate the pattern of decline and possible determinants of progression of beta cell function in patients with latent autoimmune diabetes of adult onset (LADA).	The pattern of C-peptide decline was biphasic, with a rapid drop followed by a slow one, and about a quarter of LADA cases developed beta-cell dysfunction within the first 8 years of evolution.
Autoantibodies against zinc transporter 8 further stratify the autoantibody-defined risk for type 1 diabetes in a general population of schoolchildren and exhibit distinctive isoform-binding patterns across different forms of autoimmune diabetes: results from the Karlsburg Type 1 Diabetes Risk Study.	Baumann et al., 2021	To assess the diagnostic relevance of autoantibodies against zinc transporter 8 (ZnT8) in Schoolchildren in the general population, as well as in people with autoimmune diabetes.	ZnT8 autoantibodies are also important markers in adult-onset diabetes, with a completely different reaction pattern in type 1 diabetes compared to latent autoimmune diabetes in adults, and may therefore help to differentiate between the two forms.
Detection and characterization of ZnT8 autoantibodies could help to screen for latent autoimmune diabetes in adult-onset patients with type 2 phenotype	Trabucchi et al., 2011	To evaluate the prevalence of ZnT8A in adult patients with initially classified type 2 diabetes and to characterize the recognized epitopes. by these autoantibodies	Argentine diabetic patients, initially classified as type 2, who should actually be diagnosed as LADA, highlight the importance of including the assessment of this marker in the conventional panel of exams.
Autoantibodies against ZnT8 are rare in	Heneberg et al., 2018	To assess the prevalence of ZnTA in patients	Quantifying ZnTA did not improve the

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Central-	Authors	Target	Conclusion
European LADA patients and absence in MODY patients, including those positive for other autoantibodies.		included patients with diabetes mellitus with LADA-like progression on insulin therapy who were either GADA and/or IA2A positive (LADA) or negative for these autoantibodies and had elevated C-peptide levels (ID-T2DM).	diagnosis of LADA. However, ZnTA positivity can be used as a negative pre-diagnostic criterion for MODY, even in the Central and Eastern European region, where other autoantibodies against pancreatic islet cells are common in patients with MODY.
Prevalence of diabetes-associated autoantibodies among patients presenting with type 2 diabetes and related metabolic differences	Moosaie et al., 2020	To explore the prevalence of autoantibodies (ZnT8A), antibodies against insulin, and antibodies against glutamic acid decarboxylase, as well as the relationship between the type and number of positive autoantibodies and the profiles. Glycemic and lipid levels in patients with LADA.	Patients with LADA positive for at least One of the autoantibodies (GAD65, ZnT8, and IAA) showed poorer glycemic control. Measuring these autoantibodies may help identify these patients and contribute to earlier glycemic control.
Bridging-type enzyme-linked immunoassay for zinc transporter 8 autoantibody measurements in adult patients with diabetes mellitus	Dunseath et al., 2015	A bridge-type ELISA to measure autoantibodies against zinc transporter 8 (ZnT8A) was evaluated in samples from 19 patients with different forms of diabetes mellitus.	The bridge-type ELISA assay is a convenient and reproducible method for the determination of ZnT8A in 31 serum samples. Measurement of ZnT8A increased the positivity of autoantibodies in adults with type 1 diabetes.
What has zinc transporter 8 autoimmunity taught us about type 1 diabetes?	Williams & Long, 2019	To analyze what autoantibodies against zinc transporter 8 (ZnT8A) have taught us about the pathophysiology, prediction, and diagnosis of type 2 diabetes mellitus. 1 (DM1) throughout the decade following its discovery	Analyzing ZnT8A epitopes and T cells before diagnosis will improve our understanding of disease pathogenesis and provide better biomarkers.

Based on the work done by MOOSAIE et al., 2021; HENEBERG et al., 2019; LI et

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al., 2020 and FADIGA et al., 2020, observe the role of ZnT8 in the diagnosis of LADA.

The question remains controversial. While some studies suggest that research on autoantibodies
Anti-ZnT8 may improve the identification of patients with late-onset autoimmune diabetes.
Others demonstrate low diagnostic sensitivity, indicating that their usefulness may be more limited.
Complementary rather than essential. Furthermore, the works agree that the LADA constitutes
a heterogeneous condition, situated between classic type 1 diabetes and type 2 diabetes,
characterized by the presence of autoantibodies and the gradual progression of cell failure
pancreatic beta cells.

The study by MOOSAIE et al. (2021) identified ZnT8A positivity in 3.4% of
Patients initially diagnosed with type 2 diabetes. Individuals positive for ZnT8A
They presented with lower body mass index, lower C-peptide levels, and poorer control.
glycemic, evidenced by higher fasting blood glucose and hemoglobin values.
Glycated saturates. The authors concluded that the combined assessment of ZnT8A, GAD65, and IAA may...
to assist in the discrimination of patients with LADA among those initially classified.
as carriers of type 2 diabetes, favoring early diagnosis and more effective management.
appropriate for the disease.

However, the results obtained by HENEBERG et al. (2019) differ substantially.
In this study, the majority of patients with LADA tested negative for ZnT8A.
and the diagnostic sensitivity of the marker was only 18–20%. The authors noted that
Patients who tested positive for ZnT8A had a lower BMI than individuals who tested positive for ZnT8A.
only for other autoantibodies, suggesting a phenotype closer to autoimmune diabetes.
classic. However, they concluded that quantifying ZnT8A did not improve the diagnosis of
LADA.

The findings of LI et al. (2020) provide an important context for evaluating the relevance of
immunological markers in LADA. Although the study primarily evaluated GADA and
Not ZnT8A, the authors demonstrated that elevated titers of autoantibodies are strongly
associated with the progression of ÿ-cell failure. Patients with higher titers of
GADA patients showed a more accelerated decline in pancreatic function and a higher risk of loss of
endogenous insulin secretion. These results reinforce the importance of autoantibodies.
as markers of autoimmune activity and suggest that the identification of autoantibodies
Additional tests, such as ZnT8A, can contribute to characterizing subgroups of patients with specific profiles.
More aggressive autoimmune disease.

Similarly, FADIGA et al. (2020) demonstrated that patients with diabetes

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Classic autoimmune diseases showed a higher number of positive autoantibodies when compared to individuals with LADA, which reflects a more intense autoimmune process. Although the study did not include an assessment of ZnT8A, its results corroborate the notion. that the quantity and profile of autoantibodies influence the clinical expression of the disease. Thus, ZnT8A can be interpreted as yet another potential marker for characterization. immunological effects of LADA, especially when used in conjunction with other autoantibodies. already established, such as GADA and IA-2A.

Taken together, the studies indicate that ZnT8A should not be considered an isolated marker. for the diagnosis of LADA. While MOOSAIE et al. (2021) point to benefits in their complementary use to identify hidden cases of autoimmune diabetes among patients classified as type 2 diabetes, HENEBERG et al. (2019) demonstrate low sensitivity. diagnostic, which limits its application as a primary screening tool. Still Thus, the presence of ZnT8A appears to be associated with characteristics more compatible with autoimmunity, such as lower BMI and lower functional reserve of ÿ cells, suggesting that their The main contribution is to increase the specificity of the immunological characterization of LADA. when used in conjunction with other autoantibodies. In this way, the evidence The evidence available in the analyzed articles supports the role of ZnT8A as a biomarker. complementary, but not a substitute, in the differential diagnosis between LADA and type 2 diabetes. The articles published by TRABUCCHI et al. (2012); DUNSEATH et al. (2015); BAUMANN et al. (2020) and HENEBERG et al. (2019) converge to demonstrate that the Autoantibodies against zinc transporter 8 (ZnT8A) constitute a marker. important complement for the identification of pancreatic autoimmunity in patients with LADA, especially in those who could initially be classified as having type 2 diabetes. The study of TRABUCCHI et al. (2012) showed that 10.7% of adult patients initially Those diagnosed with type 2 diabetes had a positive ZnT8A test. Among individuals with In detectable autoimmunity, ZnT8A was the second most prevalent marker (48.3%), behind only from GADA (56.7%). A particularly relevant finding was that 7.0% of patients They tested positive exclusively for ZnT8A, with no other autoantibodies detectable. indicating that its inclusion allows for the identification of LADA cases that would otherwise be missed by dashboards. traditional methods based solely on GADA and IA-2A. In addition, the ZnT8A-Trp325 variant was... most frequently identified in this adult population.

Regarding concordance, DUNSEATH et al. (2015) observed positivity for ZnT8A in

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31.4% of patients with LADA. Although the main objective of the study was to validate a
Using the ELISA method for detecting these autoantibodies, the results confirmed that a
A significant proportion of individuals with LADA exhibit an autoimmune response against ZnT8.
The authors also demonstrated that the combination of ZnT8A with other markers of
Autoimmunity increases the detection of pancreatic autoimmune disease, reinforcing its value.
complementary diagnosis.

The work of BAUMANN et al. (2020) adds an important perspective by demonstrating
that the recognition pattern of ZnT8 isoforms differs between classic type 1 diabetes
and LADA. While individuals with type 1 diabetes showed reactivity against multiple
Of the ZnT8 variants, only 10% of patients with LADA were positive for ZnT8A, and
None of them showed simultaneous reactivity against the three isoforms evaluated. Furthermore,
The autoimmune response in LADA was shown to be predominantly restricted to the ZnT8W variant.
The authors suggest that this immunological difference may reflect pathogenic mechanisms.
Distinct differences exist between the two forms of autoimmune diabetes, and the analysis of reactivity patterns...
Testing for ZnT8 can aid in the differential diagnosis between late-onset type 1 diabetes and LADA.

Regarding the diagnosis of LADA, the data presented by HENEBERG et al. (2019)
They suggest that ZnT8A may act as a complementary marker to autoantibodies.
classic cases, increasing the detection of autoimmune diabetes cases that might otherwise remain hidden.
not classified when only GADA, IA-2A, and IAA are investigated. However,
Unlike GADA — considered the main marker of LADA — the evidence
The availability of ZnT8A is still limited and heterogeneous. Therefore, ZnT8A must be
interpreted as an additional marker, capable of enhancing immunological characterization
of patients, but there is still not enough evidence to consider it an isolated marker.
or definitive for the diagnosis of LADA.

When the studies are analyzed together, there is a consensus that ZnT8A does not
It replaces classic markers, especially the GADA, but increases sensitivity.
diagnostic for the detection of autoimmunity in adults. TRABUCCHI et al. (2012) argue
that a minimum panel for LADA screening must include GADA and ZnT8A-
Arg-Trp325, precisely because some patients present ZnT8A as the only marker.
detectable.

Therefore, the results of the articles indicate that the ZnT8 gene/protein is relevant.
Diagnosis is primarily made through the detection of anti-ZnT8A autoantibodies. These
Autoantibodies broaden the identification of patients with LADA, allowing for recognition

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individuals who would be incorrectly classified as having type 2 diabetes and still present
Additional information on the immunological profile of the disease. The main contribution of ZnT8.
for the diagnosis of LADA, its role as a complementary marker is therefore crucial.
pancreatic autoimmunity, which increases the ability to screen and characterize it.
adult patients with autoimmune diabetes.

FINAL CONSIDERATIONS

It is expected that the literature review will allow for an understanding of the relevance of antibodies against
Zinc transporter 8 (ZnT8) as a complementary tool in differential diagnosis.
between Latent Autoimmune Diabetes in Adults (LADA) and Type 2 Diabetes Mellitus (DM2).
Considering the overlap in clinical characteristics between these conditions, it is predicted that the
Selected studies highlight the importance of investigating immunological markers.
for a more accurate diagnostic classification of patients.
Additionally, it is expected that evidence demonstrating the potential of the anti- antibody will be identified.
ZnT8 as a complementary marker in the detection of the autoimmune component present in
LADA, especially when used in combination with other autoantibodies related to
autoimmune diabetes, such as anti-GAD and anti-IA-2. This approach may contribute to
to increase diagnostic sensitivity and to identify early individuals who, although
initially classified as having type 2 diabetes, they present compatible characteristics.
with autoimmune diabetes.

Thus, the predicted results are promising, indicating that the inclusion of anti-ZnT8
in laboratory evaluation it can represent an important complementary resource for the
differential diagnosis between LADA and type 2 diabetes. It is also expected that the findings will reinforce the
The relevance of this biomarker for improving diagnostic accuracy, contributing to
the adoption of more appropriate and individualized therapeutic strategies, in addition to expanding the
scientific knowledge about its application in clinical practice.

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