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Case Report **OPEN ACCESS**

The diagnosis of LADA diabetes in a low-resource country: A Peruvian case series

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ABSTRACT

Introduction: Diabetes mellitus (DM) is a global public health concern, affecting 10% of adults. Among its variants, latent autoimmune diabetes in adults (LADA) accounts for 3% to 11% of cases. Limited awareness and high testing costs contribute to misdiagnosis and inadequate treatment, increasing the risk of chronic complications.

Design: A cases series.

Methods: Fifteen Peruvian patients with LADA were studied to describe their clinical presentation, diagnosis, and treatment.

Results: The average age was 36.2 years, with a mean disease duration of 5.6 years. All patients presented with acute symptoms, and their mean body mass index at diagnosis was 23.3 kg/m^2. Glycemic control was achieved with an average daily insulin dose of 0.96 IU/kg. None of the patients had access to capillary glucose self-monitoring or continuous glucose monitoring, as all were living in poverty or extreme poverty.

Conclusions: LADA is an uncommon form of early-onset DM whose diagnosis and treatment in resource-limited countries are impacted by socioeconomic conditions. Therefore, we propose a clinical algorithm for managing this condition in low-resource settings.

Keywords: latent autoimmune diabetes in adults, diabetes mellitus, insulin, diabetes complications, C-peptide, resource-limited settings

INTRODUCTION

Diabetes mellitus (DM) is characterized by persistently elevated blood glucose levels [1] and represents a serious threat to public health worldwide [2]. According to the International Diabetes Federation, 10% of adults aged 20 to 79 have DM, with more than 75% of these individuals living in low- and middle-income countries [3]. In addition to the classical forms of diabetes, such as type 1 (T1DM) and type 2 DM (T2DM), there are other less common variants, including latent autoimmune diabetes in adults (LADA), which is an autoimmune form of DM that begins in adulthood [2, 4], also known as type 1.5 DM or slow-progressing T1DM [5]. It accounts for between 3% and 11% of the adult population with DM [2, 6], and 8.3% in the Western Pacific Region [7]. It affects men and women similarly, primarily those aged between 30 and 49 years (50%) [8].

LADA typically manifests after the age of 30 and affects individuals with a normal body mass index (BMI) or those who are overweight [4, 9]. In these patients, other components of the metabolic syndrome may occur, such as an elevated waist-to-hip ratio, hypertension (HTN), and dyslipidemia, with a prevalence lower than that seen in T2DM but higher than in T1DM [9]. LADA is associated with the presence of antibodies against glutamic acid decarboxylase (GADA) and other antibodies directed against pancreatic islets, as well as other autoimmune diseases, such as autoimmune thyroiditis, type A gastritis, and vitamin B12 deficiency [4, 9, 10].

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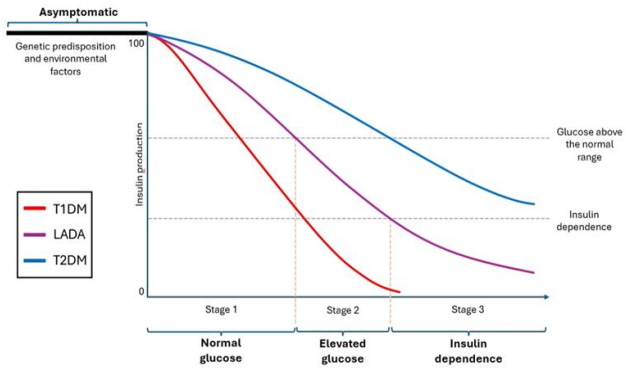

Figure 1. Differences in pancreatic insulin secretion loss among different types of diabetes (Source: Authors' own elaboration)

The development of LADA can occur over a period ranging from months to years before the onset of symptoms, with a slower progression to insulin dependence compared to T1DM [9] (**Figure 1**). Insulin secretion is reduced, as evidenced by low C-peptide levels, and progressively declines, although at a slower rate than in T1DM and faster than in T2DM. Despite this, the frequency of ketoacidosis at the time of diagnosis is low [9], unlike in T1DM. In those with an earlier onset of LADA, insulin resistance is lower, as is the residual function of β cells [11].

Glycemic control in patients with LADA is poorer compared to those with T2DM, as evidenced by higher levels of hemoglobin A1c (HbA1c) [9]. LADA often requires early insulin therapy, although not necessarily from the outset, which can lead to confusion with T2DM (**Figure 2**). Additionally, it is associated with a high prevalence of microvascular complications and cardiovascular diseases (CVDs) [4, 9].

According to the 2018 census, there are approximately 50,000 people aged 20 to 79 in the Province of Chepén [12]. Of these, it is estimated that around 5,000 have diabetes, and among them, about 415 would be present with LADA. The limited awareness of this condition, along with the high cost of the necessary diagnostic tests, such as measuring C-peptide and antibodies, may contribute to underdiagnosis. This, in turn, leads to inadequate management of LADA, increasing the risk of chronic complications, which diminishes the patient's quality of life and raises treatment costs [8].

The aim of this manuscript is to understand the clinical, epidemiological, and socioeconomic characteristics of patients with LADA in our setting, with the goal of generating evidence that can optimize diagnostic and therapeutic resources in low-income environments, thereby improving the prognosis for patients with LADA.

METHODS

Study Design

This is a retrospective case series describing the clinical presentation, diagnosis, and treatment of patients with LADA.

Participants

15 patients with LADA treated at the Chepén Support Hospital, a public second-level care hospital, between 2022 and 2024.

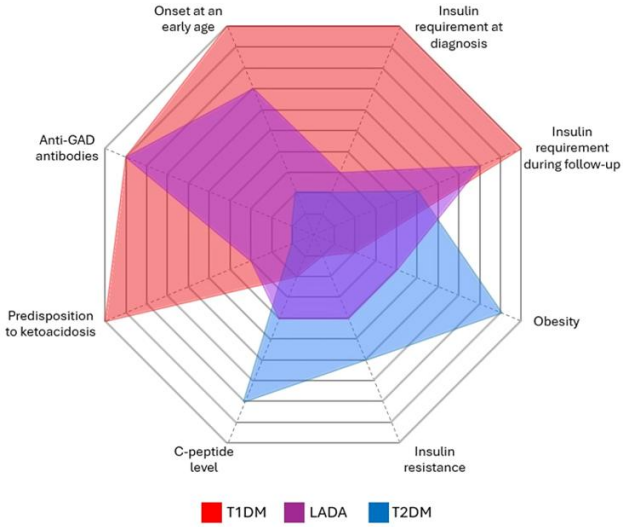

Figure 2. Spider chart highlighting the differences between T1DM, T2DM, and LADA (Source: Authors' own elaboration)

Procedures and Assessments

Information was collected from the care records in medical history during their outpatient visits. For diagnostic and treatment purposes, LADA was defined as those patients who met at least two of the Fourlanos criteria [13] and who required an insulin dose greater than 0.5 UI/kg/day for glycemic control.

The variables evaluated in all patients included epidemiological, clinical, paraclinical, and socioeconomic characteristics, such as sex, age, year of diabetes diagnosis, duration of symptoms prior to diagnosis, previous weight, personal or family history of autoimmunity, family history of cardio-metabolic conditions, previous episodes of ketoacidosis or hypoglycemia, comorbidities, current weight, height, BMI, abdominal circumference, presence of skin tags and acanthosis, complete blood count, average blood glucose without treatment, HbA1c without treatment, lipid and liver profiles, renal function, thyroid function, hepatic steatosis, cardiovascular risk assessed using the PREVENT calculator (Predicting Risk of cardiovascular disease EVENTs) from the American Heart Association [14, 15], use of oral antidiabetic agents for more than six months, insulin dosage required to achieve glycemic control according to the American Diabetes Association [16], insulin regimen, availability of a glucometer, location where glucose is measured, frequency of glucose measurement, working family members, total number of family members, and total monthly family income, as well as family support and others (**Appendix A**).

Ethical Considerations

This study was reviewed and approved by the Institutional Ethics Committee of the Chepén Support Hospital and the Faculty of Medicine at the National University of Trujillo. As this was a retrospective cases series involving the review of medical records, informed consent was not obtained.

RESULTS

A total of 15 patients with LADA were included, of whom 5 were male and 10 were female. The average age of the participants was 36.2 years. To date, they have an average

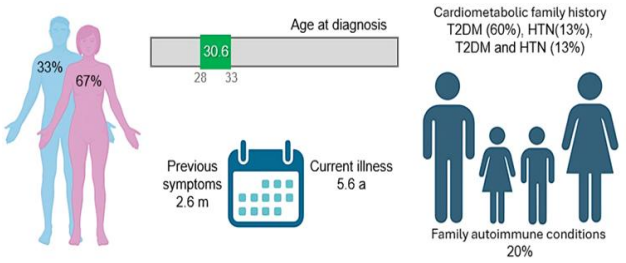

Figure 3. Demographic characteristics of study patients (Source: Authors' own elaboration)

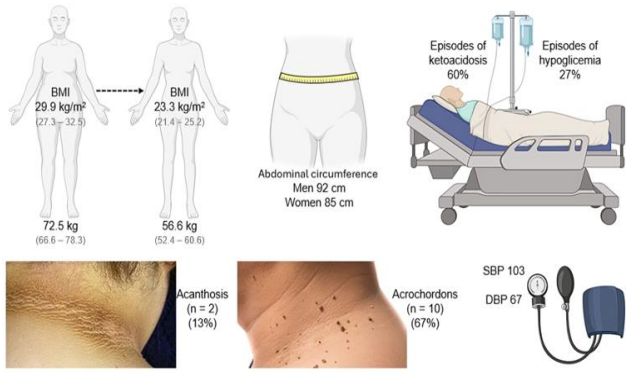

Figure 4. Clinical characteristics of study patients (Source: Authors' own elaboration)

disease duration of 5.6 years. The average age at diagnosis was 30.6 years. Before receiving the diagnosis of DM, all experienced symptoms such as polyuria, polydipsia, blurred vision, and fatigue for an average of 2.6 months. No personal history of autoimmune diseases was reported, and 3 patients (20%) reported a family history of autoimmunity (sister with probable LADA, niece with hyperthyroidism, sister with hypothyroidism). Among the family history of cardiometabolic conditions, 9 patients (60%) reported only T2DM, 2 (13%) reported only HTN, 2 reported both T2DM and HTN, and 2 did not report any condition. One patient died at the age of 41, 12 months after follow-up, due to acute myocardial infarction. These demographic characteristics are summarized in **Figure 3**.

In 2 patients, acanthosis nigricans was found, and 10 patients had acrochordons. The average weight before the onset of the disease was 72.5 kg. The average weight loss was 16 kg. The current average weight is 56.5 kg, and the average height is 1.56 m. The BMI prior to diagnosis was 29.9 kg/m^2, and after weight loss due to the disease, it was 23.3 kg/m^2. The average abdominal circumference was 87 cm, with 92 cm in males and 85 cm in females. The average systolic blood pressure (SBP) was 103 mmHg, and the average diastolic blood pressure (DBP) was 67 mmHg. Among the acute complications, 9 patients (60%) experienced ketoacidosis at some point, and 4 patients (27%) experienced hypoglycemia at some time. These clinical characteristics are summarized in **Figure 4**.

The paraclinical examinations are shown in **Table 1**.

A summary of these tests and the associated complications is presented in **Figure 5**.

All patients met at least 2 of the Fourlanos criteria. With the exception of 1 patient who was correctly diagnosed, the other 14 patients in the study (93%) had previously received a diagnosis of T2DM and had been treated with oral antidiabetic medications for an average of 27 months. At the time of the study, all these patients had achieved glycemic control targets

Table 1. Characteristics of auxiliary tests and associated complications of the study patients

Parameter	Medium	Reference range
Leukocytes (cells/µL)	8,537	5,000-10,000
Neutrophils (%)	62.6	40-60
Basophils (%)	0.4	0.5-1.0
Eosinophils (%)	2.7	1-4
Monocytes (%)	5.1	2-8
Lymphocytes (%)	30.0	20-40
Hb (g/dL)	13.1	> 12 (female) & > 13 (male)
MCV (fL)	90	80-100
MCH (mg/dL)	29	27-33
RDW (%)	14.0	11-15
Platelets (units/µL)	330,866	150,000-450,000
NLR	2.3	1-3
PLR	141	90-210
Fasting glucose without treatment (mg/dL)	336	70-100
HbA1c without treatment (%)	13.3	4.5-5.7
Maximum glucose reached (mg/dL)	468	-
Total cholesterol (mg/dL)	202	< 200
HDL cholesterol (mg/dL)	39	> 50 (female) & > 40 (male)
LDL cholesterol (mg/dL)	116	< 100
Triglycerides (mg/dL)	208	< 150
AST (UI/L)	32	< 30
ALT (UI/L)	39	< 30
Serum proteins (mg/dL)	7.1	6.0-8.3
Serum albumin (mg/dL)	4.3	3.5-5.0
Serum creatinine (mg/dL)	0.89	0.7-1.3 (male) & 0.6-1.1 (female)
eGFR (mL/min/1.73m^2)	98	90-120
Urine proteins (mg/24 hours)	386	< 80
TSH (mUI/L)	2.6	0.4-4.0
CVD risk (%)	3.6	-
ASCVD risk (%)	2.2	-
HF risk (%)	1.4	-

Note. ALT: Alanine aminotransferase; ASCVD: Atherosclerotic cardiovascular disease; AST: Aspartate aminotransferase; CVD: Cardiovascular disease; eGFR: Estimated glomerular filtration rate; Hb: Haemoglobin; HDL: High-density lipoprotein; HF: Heart failure; LDL: Low-density lipoprotein; MCH: Mean corpuscular hemoglobin; MCV: Mean corpuscular volume; NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; RDW: Red cell distribution width; TSH: Thyroidstimulating hormone

using insulin at an average dose of 0.96 IU/kg/day, primarily in a basal-bolus regimen (87%). These characteristics of diagnosis and treatment are summarized in **Figure 6**.

Among the study patients, few had a glucometer (27%), and none had test strips, so glycemic monitoring was entirely conducted during medical consultations, with an average frequency of 14 days (95% confidence interval = 9-19). Seven of the patients (47%) are the economic providers for their households. The socioeconomic characteristics are summarized in **Figure 7**.

DISCUSSION

In 2005, the Diabetes Immunology Society established three criteria for the diagnosis of LADA: onset of the disease above the age of 30, presence of any antibody against the islets, and absence of the need for insulin for at least 6 months after diagnosis [17].

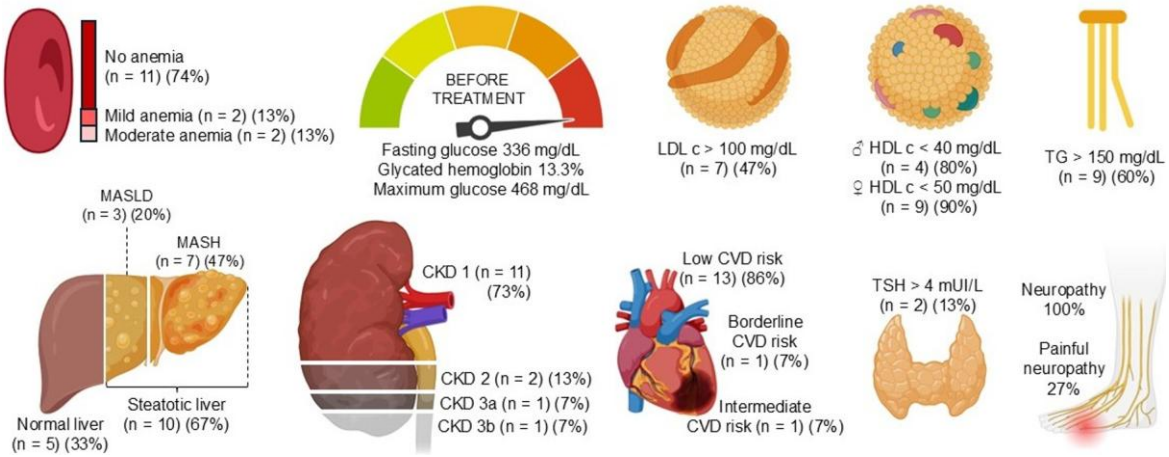

Figure 5. Summary of auxiliary tests and associated complications of study patients (ASCVD: Atherosclerotic cardiovascular disease; CKD: Chronic kidney disease; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; MASH: Metabolic dysfunction-associated steatohepatitis; MASLD: Metabolic dysfunction-associated fatty liver disease; TG: Triglycerides; & TSH: Thyroid-stimulating hormone) (Source: Authors' own elaboration)

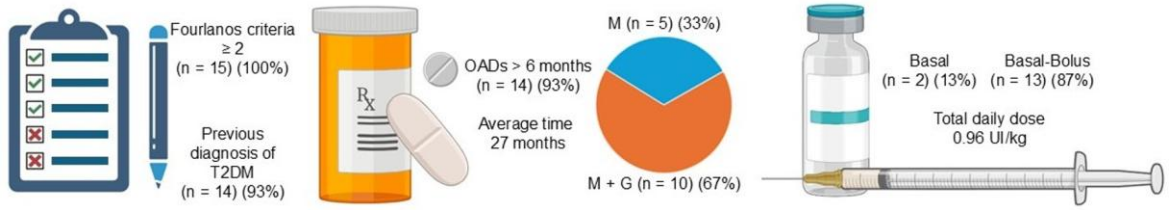

Figure 6. Characteristics of the diagnosis and treatment of study patients (G: Glibenclamide; IU: International units; kg: kilogram; M: Metformin; OAD: Oral antihyperglycemic agents) (Source: Authors' own elaboration)

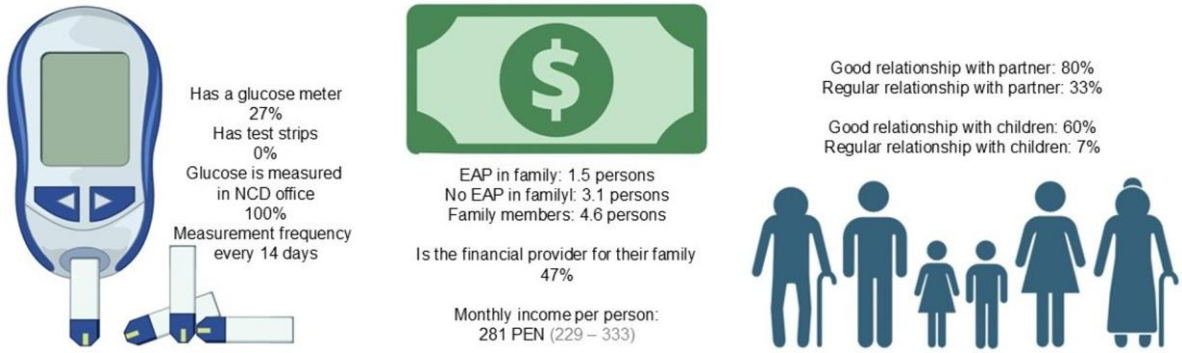

Figure 7. Socio-economic characteristics of the study patients (EAP: Economically active population; NCD: Non-communicable chronic diseases) (Source: Authors' own elaboration)

Table 2. Fourlanos criteria (2006) for LADA diagnosis

Parameter
1. Age of onset less than 50 years
2. Acute symptoms
3. BMI less than 25 kg/m²
4. Personal history of autoimmune disease
5. Family history of autoimmune disease

In 2006, Fourlanos and colleagues identified five clinical characteristics that were more common in LADA than in T2DM at the time of diagnosis, which are shown in **Table 2**.

The presence of at least two of these characteristics demonstrated a sensitivity of 90% and a specificity of 71% for identifying LADA, with a negative predictive value of 99% for a score of one or less [13]. In our study, at the time of diagnosis, all patients were under 50 years old, with three of them aged between 20 and 25 years; all experienced acute symptoms for 2.6 months; and 67% had a BMI below 25 kg/m². Three patients reported autoimmunity, although this could not be confirmed due to economic limitations.

There were observed cases of acrochordons and some cases of acanthosis in patients with a higher BMI. Several studies have shown that insulin resistance in patients with LADA is lower than that observed in patients with T2DM but comparable to that of patients with T1DM. Additionally, other studies suggest that insulin resistance may be similar to that found in T2DM. It can be inferred that insulin resistance is a crucial factor in the pathophysiology of LADA [18, 19].

Ketoacidosis is not typically the usual form of onset in patients with LADA [20]. In our study, although 60% of patients experienced ketoacidosis at least once during the course of the disease, none presented it at the time of diagnosis. The risk of

hypoglycemia is high due to the concomitant dysfunction of alpha cells, resulting in an altered glucagon response to low blood glucose levels [9]. We observed that 27% of patients had experienced at least one episode of hypoglycemia in their lifetime.

At the time of LADA diagnosis, chronic complications of the disease are not usually found [21]. In our population, despite having an average of 5.6 years of poor glycemic control, it was observed that 86% of patients had an estimated glomerular filtration rate of 60 ml/min/1.73 m^2 or higher, and 86% presented a low cardiovascular risk for the next 10 years. Although all patients showed clinical signs of neuropathy, 74% did not experience neuropathic pain. It is noteworthy that 87% of our patients had a family history of hypertension and T2DM, which could imply a higher risk of developing microvascular and macrovascular complications during follow-up [22].

Studies show that, in the long term, there is no significant difference between LADA and T2DM regarding the incidence of retinopathy (75% vs. 74.3%) and neuropathy (62.5% vs. 66.9%). However, nephropathy was more common in patients with LADA (25% vs. 11.5%), while diabetic foot was observed less frequently (12.5% vs. 33.1%) [8]. During follow-up, patients with LADA experienced 25% more microvascular complications compared to patients with T2DM, likely due to less effective glycemic control [23]. In fact, one of our patients died at the age of 41 from an acute myocardial infarction.

It is recommended to measure baseline C-peptide levels at the onset and to perform repeat measurements every 6 months [21, 24]. Initially, C-peptide levels are typically low, ranging from 0.9 to 1.8 ng/mL, with a progressive decrease observed in subsequent measurements [9]. Additionally, it is advised to measure islet autoantibodies, primarily GADA [9]; however, these antibodies lack high specificity, which means that the definition of autoantibody positivity is not unequivocal [25]. None of the patients in the study underwent C-peptide measurement or autoantibody detection due to economic limitations.

Considering that poverty is defined as a per capita income below the cost of a basic consumption basket of food and non-food items (446 PEN per month per inhabitant for the year 2023), and extreme poverty as a per capita income below the cost of a basic food basket (251 PEN per month per inhabitant for the year 2023) [26, 27], it was found that eight of our patients were living in poverty and seven in extreme poverty. This situation is relevant, as socioeconomic status can significantly affect the management of diabetes. Achieving adequate control of DM poses a challenge in this context due to financial difficulties that limit access to quality medical care, as well as to medications, necessary supplies, and healthy foods [28].

It has been reported that 10% of adults initially diagnosed with T2DM have been classified as patients with LADA [8, 29]. In our population, nearly all patients had previously received a diagnosis of T2DM. The unofficial nominal registry of the non-communicable disease health strategy in our area includes 600 patients with T2DM, indicating that the misdiagnosis of T2DM has occurred in 2.3% of them so far. This may suggest that there is a significant number of underdiagnosed patients.

The goal of managing LADA is to preserve the ability to produce insulin [21], prevent acute and chronic complications, and improve the quality of life for individuals living with this disease, starting with the adoption of healthy lifestyles [9]. Although insulin is generally not required during the first 6 months after diagnosis [8], insulin therapy becomes crucial to control hyperglycemia, prevent ketoacidosis, and preserve β cells. The appropriate time to initiate therapy can be determined through the measurement of basal C-peptide levels [9, 21]. In our study, it was observed that poor glycemic control was not primarily due to the lack of incorporation of healthy lifestyle habits but rather to a lack of awareness about the disease and errors in the previously prescribed pharmacotherapy, which differs from what has been described in patients with T2DM [30].

Three categories have been proposed to establish treatment recommendations: for C-peptide levels < 0.9 ng/mL, a multiple insulin injection regimen is recommended; for C-peptide levels between 0.9 and 2.1 ng/mL, an algorithm similar to that used in T2DM according to the ADA 2024 is suggested, starting with basal insulin in combination with other therapies and avoiding sulfonylureas; and for C-peptide levels > 2.1 ng/mL, the aforementioned algorithm can be used, but considering the potential progression of LADA through monitoring C-peptide levels to adjust treatment. Insulin dosage adjustments can follow the recommended guidelines for T2DM, especially when C-peptide levels are 0.9 ng/mL or higher [9, 21].

Although intensive insulin therapy is essential for the recovery and maintenance of β-cell function in individuals with T2DM, no studies have yet been reported on the intensification of insulin in patients with LADA [11]. Given the high risk of hypoglycemia, it is crucial to continuously educate patients about the accurate administration of insulin doses, the correct injection technique, regular self-monitoring of blood glucose levels, and the prompt correction of hypoglycemic episodes [9].

Other medications can be used, either alone or in combination with insulin, depending on β-cell reserve, although many lack formal regulatory approval [9]. Insulin sensitizers are essential due to the increasing insulin resistance in individuals with LADA, which is often associated with overweight and obesity [9]. Metformin is not specifically approved for LADA, but its safety profile and cost have promoted its use in adults [9, 11]. Thiazolidinediones may help preserve β-cell function, although they carry risks of fractures, macular edema, weight gain, and have limited efficacy in thin patients [9, 11]. On the other hand, sulfonylureas contribute to poor metabolic control and a faster deterioration of β-cell activity, so their use is not recommended in these patients [9, 31].

Dipeptidyl peptidase 4 inhibitors are well tolerated and reduce glucose levels in patients with LADA, although there is no conclusive evidence regarding the preservation of β-cells [9, 11]. Glucagon-like peptide-1 receptor agonists offer significant metabolic, cardiovascular, and renal benefits and may preserve β-cell function, especially in patients with residual β-cell function [9, 11, 32]. Sodium-glucose cotransporter type 2 inhibitors (SGLT-2i) have been shown to improve glycemic control, although their use has generated controversy due to the increased risk of diabetic ketoacidosis (DKA). However, their cardiovascular, renal, and metabolic benefits, especially in patients with a BMI of 27 kg/m^2 or higher, when combined with an adequate dose of insulin, make them a suitable option [9, 11, 32]. Euglycemic DKA is a rare complication associated with the use of SGLT-2i [33]. Individuals with a lower BMI and reduced glycogen stores may be more predisposed to this complication [34]. Therefore, if the use of SGLT-2i is considered

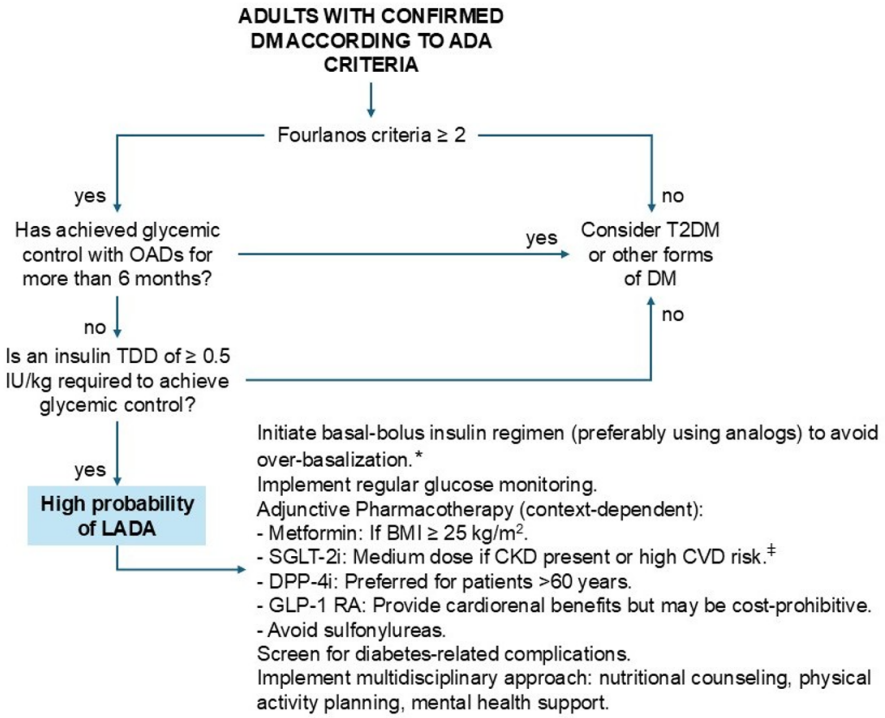

Figure 8. Proposed diagnostic and treatment algorithm for patients with LADA in resource-limited settings. ADA: American Diabetes Association; DPP-4i: Dipeptidyl peptidase-4 inhibitors; GLP-1 RA: Glucagon-like peptide-1 receptor agonists; OAD: Oral antidiabetic drugs; SGLT-2i: Sodium-glucose cotransporter type 2 inhibitors; TDD: Total daily dose.

* Over-basalization may occur, especially when the total daily dose exceeds 0.5 UI/kg/day, during episodes of warned or unwarned hypoglycemia, or in situations where there is a significant difference between bedtime and waking glucose levels, or between postprandial and preprandial glucose levels.

ǂiSGLT-2 at moderate doses: dapagliflozin 5 mg daily or empagliflozin 10 mg daily) (Source: Authors' own elaboration)

in patients with LADA, it should be carried out with caution and constant monitoring [35].

In 2023, the poverty rate in Peru was 29.0%, while extreme poverty reached 5.7%. This situation is recorded in the context of economic recession, adverse climatic shocks, and still high inflationary pressures on the basic food basket [36]. In the context of addressing LADA, the lack of specific tests, such as C-peptide measurement and islet autoantibodies, greatly limits the possibility of confirming the diagnosis of LADA in most affected individuals. Therefore, in **Figure 8**, we present an algorithm for the diagnosis and treatment of these cases in resource-limited settings.

Glucose variability (GV) contributes to diabetes-related complications. Continuous glucose monitoring (CGM) significantly improves glycemic control, especially in patients with T1DM, achieving a notable reduction in GV, severe hypoglycemia episodes, and HbA1c levels, as well as an increase in time in range (TIR) [37, 38]. It has been observed that real-time CGM outperforms intermittently scanned CGM in these aspects [39]. Both patients with T1DM and those with LADA show comparable TIR and GV, particularly in insulin-dependent cases of LADA [40]. Although evidence regarding the ideal glycemic monitoring type for patients with LADA is limited, CGM is recommended. However, given the previously described economic limitations, this is practically unfeasible in our setting. Many patients face significant difficulties in performing glucose self-monitoring, as those who have a glucometer often lack test strips and must rely on going to the hospital or pharmacy to measure their capillary glucose. In many cases, it is unthinkable to measure glucose when experiencing symptoms of nocturnal hypoglycemia, forcing patients to go to the hospital's emergency room.

Regarding the limitations, none of the patients underwent C-peptide and GADA measurements, as their high cost could not be borne by the patients due to the previously described conditions. For the same reasons, we did not have the ability to evaluate antibodies to detect autoimmunity or to study the urine albumin/creatinine ratio, limiting ourselves to determining proteinuria in a 24-hour urine collection.

In conclusion, LADA is a form of early-onset diabetes that presents serious challenges in its diagnosis and treatment, especially in resource-limited settings. The lack of access to diagnostic tools, monitoring, and appropriate treatments increases the incidence of acute and chronic complications. Therefore, it is essential to improve education and resources dedicated to the early detection and management of this condition. Identifying specific clinical characteristics and strengthening public health policies are crucial to improving the quality of life for these patients.

Author contributions: **JQA**: conceptualization, methodology, investigation, resources, data curation, formal analysis, writing – original draft, supervision, project administration; **MDV**: resources, investigation, data curation, writing – original draft; **SIN**: investigation, writing – review & editing; **EGO**: investigation, writing – review & editing; **SPL**: investigation, writing – original draft; **CQG**: investigation, writing – original draft; **LCU**: investigation, writing – review & editing; **JPI**: formal analysis, investigation, writing – review & editing; **EAL**: investigation, writing – review & editing; **EAU**: investigation, writing – review & editing; **AAH**: investigation, writing – review & editing; **MCZ**: formal analysis, investigation, writing – review & editing. All authors have agreed with the results and conclusions.

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Ethical statement: This study was approved by the Institutional Ethics Committee of the Chepén Support Hospital and the Faculty of Medicine at the National University of Trujillo on 2 September 2024 with approval number 215-2024-UNT-FM-C.E.

Declaration of interest: No conflict of interest is declared by the authors.

Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

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APPENDIX A

Table A1.

No	Age	YD	AD	PSD	WPD	DCI	FA	FCH	Any DKA?	Any HG?	ACA	ACR	W	H	BMI-P	BMI (kg/m²)	AC
1	38	2021	35	2.0	80	3	Unknown	T2DM	Yes	No	No	Yes	52	1.59	31.6	20.6	90
2	38	2021	35	4.0	67	3	Unknown	No	Yes	Yes	No	Yes	59	1.47	31.0	27.3	86
3	31	2023	30	2.5	67	1	Unknown	T2DM	No	No	No	No	52	1.60	26.2	20.3	97
4	29	2017	22	2.0	67	7	Unknown	T2DM	No	No	No	Yes	53	1.50	29.8	23.6	92
5	33	2015	24	3.0	63	9	Unknown	T2DM	Yes	Yes	No	No	51	1.56	25.9	21.0	82
6	39	2017	32	1.5	72	7	Unknown	T2DM	No	No	No	Yes	62	1.55	30.0	25.8	85
7	32	2020	28	1.0	56	4	Unknown	T2DM	Yes	No	No	No	53	1.60	21.9	20.7	81
8	46	2012	34	2.0	85	12	Sister with hypothyroidism	T2DM, HTN	No	No	No	Yes	64	1.65	31.2	23.5	92
9	36	2020	32	3.0	88	4	Unknown	T2DM	Yes	No	Yes	Yes	76	1.55	36.6	31.6	91
10	42	2020	38	2.0	96	4	Unknown	HTN	Yes	No	Yes	Yes	65	1.50	42.7	28.9	90
11	41	2016	33	5.0	72	8	Unknown	HTN	Yes	Yes	No	Yes	49	1.64	26.8	18.2	83
12	28	2017	21	4.0	65	7	Sister with LADA	T2DM	Yes	Yes	No	No	54	1.58	26.0	21.6	81
13	40	2014	30	2.3	80	10	Unknown	No	No	No	No	Yes	51	1.56	32.9	21.0	82
14	40	2019	35	3.0	55	5	Niece with hyperthyroidism	T2DM	Yes	No	No	No	44	1.48	25.1	20.1	80
15	30	2024	30	2.0	75	0	Unknown	T2DM, HTN	No	No	No	Yes	63	1.57	30.4	25.6	96

Note. AC: Abdominal circumference (cm); ACA: Acanthosis; ACR: Acrochordons; AD: Age at diagnosis (years); BMI-P: BMI prior to diagnosis (kg/m²); DCI: Duration of current illness (years); FA: Family autoimmunity; FCH: Family cardiometabolic history; H: Height (m); HG: Hypoglycemia; PSD: Prior symptom duration (months); W: Weight (kg); WPD: Weight prior to diagnosis (kg); YD: Year of diagnosis

Table A2.

No	SBP	DBP	WBC	N	B	E	M	L	Hb	MCV	MCH	RDW	Plat	NLR	PLR	GLU	HbA1c	TC	HDL	LDL	TG
1	110	70	11,000	64.1	0.4	2.7	5.4	27.4	9.9	86.7	26.4	19.1	481,000	2.34	159.59	280	12.0	130	41	64	102
2	100	60	12,370	55.1	0.5	2.8	4.4	37.2	16.1	93.6	30.7	13.6	332,000	1.48	72.15	250	12.2	238	57	150	158
3	120	70	7,470	50.0	0.5	1.6	6.8	41.1	13.6	94.0	31.5	12.8	389,000	1.22	126.70	370	17.4	189	37	96	263
4	100	70	8,820	65.6	0.4	1.5	4.6	27.9	13.0	87.9	27.9	12.8	249,000	2.35	101.19	260	13.4	219	39	104	237
5	90	60	9,950	59.0	0.5	2.7	4.9	32.9	11.6	88.4	27.9	13.4	314,000	1.79	95.92	390	15.4	234	41	146	305
6	100	70	11,870	79.8	0.1	1.5	4.8	13.8	11.2	87.2	27.7	14.8	321,000	5.78	195.96	320	9.8	214	47	83	403
7	100	70	6,260	58.8	0.6	2.9	4.2	33.5	13.8	92.9	29.1	12.9	487,000	1.76	232.23	340	10.6	284	30	213	586
8	120	80	6,770	63.0	0.3	1.2	4.3	28.2	16.0	94.6	30.8	13.2	208,000	2.23	108.95	390	14.3	249	39	146	200
9	100	70	9,450	72.0	0.4	3.1	4.0	33.7	14.0	87.9	27.9	12.8	340,000	2.14	106.76	350	13.8	300	45	220	157
10	100	60	5,100	54.8	0.7	2.1	4.6	37.8	12.6	96.0	30.6	14.1	178,000	1.45	92.33	320	12.6	164	34	98	151
11	100	70	5,860	59.8	0.5	5.9	5.5	28.3	7.6	86.5	27.3	16.8	380,000	2.11	229.14	420	14.2	114	35	60	65
12	90	60	7,390	68.7	0.2	6.2	5.7	28.1	15.1	92.9	29.1	13.7	310,000	2.44	149.28	380	14.5	163	42	112	139
13	110	70	6,740	59.0	0.4	2.7	5.3	27.5	13.2	89.1	28.2	12.6	269,000	2.15	145.13	310	12.8	188	36	98	106
14	90	60	9,550	60.0	0.4	1.9	5.6	32.0	14.4	89.6	30.6	13.1	317,000	1.88	103.73	380	13.2	209	34	95	145
15	110	70	9,450	70.0	0.3	1.4	6.9	21.0	14.2	82.0	27.0	14.7	388,000	3.33	195.52	280	12.8	139	27	54	110

Note. B: Basophils; DBP: Diastolic blood pressure (mmHg); E: Eosinophils; GLU: Mean glucose without treatment; Hb: Haemoglobin; HbA1c: Glycated hemoglobin; HDL: High-density lipoprotein; L: Lymphocytes; LDL: Low-density lipoprotein; M: Monocytes; MCH: Mean corpuscular hemoglobin; MCV: Mean corpuscular volume; N: Neutrophils; NLR: Neutrophil-to-lymphocyte ratio; Plat: Platelets; PLR: Platelet-to-lymphocyte ratio; RDW: Red cell distribution width; SBP: Systolic blood pressure (mmHg); TC: Total cholesterol; TG: Triglycerides; WBC: White blood cells (cells/µL)

Table A3.

No	AST (UI/L)	ALT (UI/L)	Serum proteins (mg/dL)	Serum albumin (mg/dL)	Creatinine (mg/dL)	eGFR (mL/min/1.73 m²)	Urine proteins (mg/24 h)	TSH (mIU/L)	MASLD	CVD risk (%)	ASCVD risk (%)	HF risk (%)	Fourlanos criteria
1	15	12	5.7	3.0	0.8	116	155	3.43	No	2.1	1.3	1.0	Yes
2	24	26	7.4	5.4	0.6	118	268	1.18	Mod	2.3	1.4	1.0	Yes
3	75	86	6.6	5.1	1.0	103	372	3.10	Mod	2.6	1.8	0.9	Yes
4	61	54	5.8	3.8	0.6	125	429	2.60	Mod	2.1	1.3	0.6	Yes
5	17	27	7.7	4.6	0.8	100	775	1.90	Mod	3.1	1.8	1.0	Yes
6	13	16	7.5	3.9	1.2	59	764	1.30	No	3.4	2.0	1.4	Yes
7	51	47	7.8	4.7	0.6	122	175	2.60	Mod	4.2	2.7	0.7	Yes
8	23	26	7.4	4.6	0.9	107	275	1.80	Mod	6.6	4.9	2.2	Yes
9	38	73	6.9	4.4	1.2	60	461	2.76	Mod	4.3	2.8	1.2	Yes
10	46	85	6.6	4.1	0.8	72	190	2.90	Mod	4.0	2.3	1.5	Yes
11	25	32	7.1	3.5	2.0	42	988	1.60	Mod	8.8	4.1	5.7	Yes
12	19	19	7.1	4.0	0.8	115	360	3.20	Mod	1.6	0.9	0.8	Yes
13	21	22	6.7	4.2	0.9	112	220	1.52	Mod	3.0	1.9	0.9	Yes
14	45	45	7.4	4.7	0.5	122	180	4.80	Mod	4.2	2.3	1.4	Yes
15	11	10	9.0	4.6	0.6	133	176	4.74	No	1.6	1.1	0.5	Yes

Note. ALT: alanine aminotransferase; ASCVD: atherosclerotic cardiovascular disease; AST: aspartate aminotransferase; CVD: cardiovascular disease; eGFR: estimated glomerular filtration rate; HF: heart failure; MASLD: metabolic dysfunction-associated steatotic liver disease; Mod: moderate; TSH: thyroid-stimulating hormone

Table A4.

No	Neuropathy	Painful neuropathy	Use of OAD for more than 6 months	Duration (months)	Which ones?	Insulin regimen (Basal, BB)	Daily insulin dose for control (IU)	TDD per weight (IU/kg/day)	Previous DX	Maximum glucose	Has glucose meter?	Has test strips?
1	Yes	No	Yes	8	M	BB	54	1.04	T2DM	450	Yes	No
2	Yes	Yes	Yes	15	M, G	BB	54	0.92	T2DM	520	No	No
3	Yes	No	Yes	5	M	BB	48	0.92	T2DM	600	No	No
4	Yes	No	Yes	84	M, G	BB	48	0.91	T2DM	480	No	No
5	Yes	No	Yes	8	M, G	BB	72	1.41	T2DM	560	Yes	No
6	Yes	Yes	Yes	36	M	Basal	48	0.77	T2DM	500	No	No
7	Yes	Yes	Yes	8	M	BB	48	0.91	T2DM	410	No	No
8	Yes	No	Yes	96	M, G	BB	66	1.03	T2DM	420	Yes	No
9	Yes	No	Yes	24	M, G	Basal	48	0.63	T2DM	370	No	No
10	Yes	No	Yes	18	M, G	BB	72	1.11	T2DM	420	No	No
11	Yes	No	Yes	6	M	BB	38	0.78	T2DM	550	Yes	No
12	Yes	Yes	Yes	30	M, G	BB	42	0.78	T2DM	420	No	No
13	Yes	No	Yes	36	M, G	BB	60	1.18	T2DM	390	No	No
14	Yes	No	Yes	8	M, G	BB	54	1.23	T2DM	420	No	No
15	Yes	No	No	.	.	BB	54	0.86	.	510	No	No

Note. BB: Basal-bolus; Dx: Diagnosis; G: Glibenclamide; M: Metformine; OAD: Oral antidiabetic drug; T2DM: Type 2 diabetes mellitus; TDD: Total daily dose

Table A5.

No	Where do you measure glucose	Frequency of measurement (day)	Family: PEA	Family: Non-PEA	Total family members	Is primary breadwinner?	Total family income (PEN)	Per capita income (PEN/person)	Relationship with partner	Relationship with children	Complications / Intercurrent events
1	NCDo	14	1	3	4	Yes	1,300	325	Good	Good	
2	NCDo	7	1	5	6	No	1,200	200	Good	Good	
3	NCDo	14	2	2	4	Yes	1,400	350	Fair	Good	
4	NCDo	14	2	3	5	Yes	1,200	240	Fair	Good	
5	NCDo	7	1	2	3	No	1,200	400	Fair	Good	
6	NCDo	7	1	3	4	No	900	225	Good	Good	
7	NCDo	14	1	4	5	No	400	80	Good	Good	
8	NCDo	30	2	2	4	Yes	1,700	425	Good	Good	
9	NCDo	30	1	3	4	Yes	1,300	325	Good	Good	
10	NCDo	7	1	3	4	No	1,000	250	Fair	Good	
11	NCDo	7	1	4	5	No	1,200	240	-	-	Died at 41 years old
12	NCDo	14	1	2	3	No	1,200	400	Good	Good	
13	NCDo	14	2	3	5	Yes	1,300	260	Fair	Good	
14	NCDo	30	3	6	9	No	1,100	122	Good	Good	
15	NCDo	7	2	2	4	Yes	1,500	375	Good	-	

Note. EAP: Economically active population; NCDo: Non-Communicable Diseases office; PEN: Peruvian soles