

Glycemic Control, Drug Therapy, and Cardiovascular Risk in Older Adults with Type 2 Diabetes: A Cohort Analysis in Rosario

Relación entre el control glucémico, el tratamiento farmacológico hipoglucemiante y el riesgo cardiovascular en adultos mayores con diabetes tipo 2: análisis de una cohorte en Rosario

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ABSTRACT

Background: The global acceleration of population aging is reflected in Argentina, with projections anticipating a progressive rise in the burden of chronic diseases. The prevalence of type 2 diabetes mellitus (T2DM) increases with age; older adults constitute the largest and most complex group in terms of clinical management. Planning care strategies requires a regional characterization of this population.

Objective: The aim of this study is to describe the association between glycemic control, glucose-lowering drug therapy, and cardiovascular risk in older adults with T2DM.

Methods: We conducted a descriptive, non-interventional study of 350 functionally independent patients ≥ 60 years with T2DM, using patient laboratory records of Policlínico PAMI I in Rosario between January and December 2023. The clinical characteristics, comorbidities, glucose-lowering treatment, and glycemic control as measured by glycated hemoglobin (HbA1c) were analyzed, as well as the atherogenic indices derived from the lipid profile. Missing data were handled using multiple imputation by fully conditional specification.

Results: Two or more comorbidities were identified in 65.1% of patients, and only 7.1% had no associated comorbidities. The most common comorbidities were overweight/obesity (92.3%), hypertension (83.4%), dyslipidemia (36.6%), and cardiovascular disease (16.0%); 54.7% were receiving combination drug therapy, with metformin being the most commonly used drug (72.8%), while glucagon-like peptide-1 (GLP-1) receptor agonists and sodium-glucose cotransporter 2 (SGLT2) inhibitors accounted for only 5.7% of treatments. Adequate glycemic control was achieved by 63.2% (HbA1c $<7.5\%$), yet 15% had HbA1c $\leq 6\%$, consistent with possible overtreatment. More than half of the patients with adequate glycemic control had abnormal atherogenic indices.

Conclusion: Most patients in this cohort of older adults with T2DM achieved traditional glycemic control targets; however, utilization of hypoglycemic drugs with proven cardiovascular benefits was low, and a significant proportion of patients presented potential overtreatment and persistent residual cardiovascular risk as evidenced by abnormal atherogenic indices even in the presence of good glycemic control. These findings support a comprehensive assessment combining glycemic control and residual cardiovascular risk reduction.

Key words: Older adults - Type 2 diabetes - Cardiovascular risk - Glycemic control

RESUMEN

Introducción: La aceleración del envejecimiento poblacional global se refleja en Argentina; las proyecciones anticipan una progresión creciente en la carga de enfermedades crónicas. La prevalencia de la diabetes mellitus tipo 2 (DM2) aumenta con la edad; los adultos mayores constituyen el grupo mayoritario y más complejo para su manejo clínico. La planificación de estrategias para su cuidado requiere de la caracterización regional de esta población.

Objetivo: Describir la relación entre el control glucémico, el tratamiento farmacológico hipoglucemiante y el riesgo cardiovascular en adultos mayores con DM2.

Material y métodos: Se realizó un estudio descriptivo, no intervencionista, en 350 pacientes funcionalmente independientes, mayores de 60 años, con diagnóstico de DM2, atendidos entre enero y diciembre de 2023 en el Laboratorio del Policlínico PAMI I de Rosario. Se analizaron características clínicas, comorbilidades, tratamiento hipoglucemiante, control glucémico mediante hemog-

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lobina glicosilada (HbA1c) e índices aterogénicos derivados del perfil lipídico. Los datos faltantes del perfil lipídico fueron tratados mediante imputación múltiple.

Resultados: El 65,1% de los pacientes presentó dos o más comorbilidades y solo el 7,1% no registró comorbilidades asociadas. Predominaron el sobrepeso/obesidad (92,3%), la hipertensión arterial (83,4%), la dislipidemia (36,6%) y la enfermedad cardiovascular (16,0%). El 54,7% recibía tratamiento farmacológico combinado. La metformina fue el fármaco más utilizado (72,8%), mientras que los agonistas de los receptores del péptido semejante al glucagón tipo 1 (arGLP-1) y los inhibidores del cotransporte sodio glucosa tipo 2 (iSGLT2) representaron únicamente el 5,7% de los tratamientos. El 63,2% alcanzó un control glucémico adecuado (HbA1c <7,5%), aunque el 15% presentó HbA1c ≤6%, compatible con posible sobretratamiento. Más de la mitad de los pacientes con adecuado control glucémico presentó índices aterogénicos alterados.

Conclusión: En esta cohorte, la mayoría de los adultos mayores alcanzó las metas tradicionales de control glucémico; sin embargo, se observó una baja utilización de fármacos con beneficio cardiovascular demostrado, una proporción relevante de pacientes con posible sobretratamiento hipoglucemiante y persistencia de riesgo cardiovascular residual, evidenciada por índices aterogénicos alterados aun en presencia de buen control glucémico. Estos hallazgos respaldan una evaluación integral que combine el control de la glucemia con la reducción del riesgo cardiovascular.

Palabras clave: Adulto mayor - Diabetes tipo 2 - Riesgo cardiovascular - Control glucémico

INTRODUCTION

Population aging is a rapidly growing global phenomenon. The World Health Organization underscores that, for the first time in history, most people can expect to live beyond the age of 60 and predicts that trend will continue over the coming decades, driven by reduced mortality and healthcare advances in all regions of the world. (1) The Baseline Report for the Decade of Healthy Ageing 2021–2030 highlights the accelerating pace of population aging in low-, middle-, and high-income countries and the need to adapt health systems to respond to this demographic shift. (2) In Latin America, the population aging process continues to accelerate. According to recent estimates by the Economic Commission for Latin America and the Caribbean (ECLAC), the proportion of people aged 60 and older will increase steadily over the coming decades, reaching around 18% by 2030 and exceeding 25% by 2050. (3) In Argentina, this phenomenon has been observed since the mid-20th century, positioning the country as one of the most aged populations in the region. The 2010–2040 Population Projections published by the National Institute of Statistics and Censuses (INDEC) predict this trend will continue, with an increase in the number of older adults and a progressive rise in the burden of chronic diseases. (4) At the same time, diabetes mellitus (DM) has become one of the chronic diseases with the greatest global impact. It is a leading cause of blindness, chronic kidney disease, and cardiovascular disease, and was the ninth leading cause of death globally in 2019. (5) Type 2 diabetes mellitus (T2DM), its most common form, is characterized by insulin resistance and varying degrees of pancreatic dysfunction. Its prevalence increases significantly with age, driven by physiologic changes associated with aging, such as increased visceral adiposity, decreased lean body mass, reduced insulin sensitivity, and diminished regenerative capacity of beta cells. (6) Globally, according to the latest International Diabetes Federation (IDF) report, nearly 589 million adults aged 20 to 79 live with DM, a figure projected to reach 853 million by 2050. (7) In Argentina,

the prevalence is 14%, and data from the latest National Risk Factor Survey indicate a steady increase over the past few decades. (8)

Traditionally, excess weight has been considered the primary modifiable risk factor for T2DM. However, recent evidence indicates that age has an independent and strong effect on the incidence of this disease, even in individuals with a normal body mass index (BMI). (9) Consequently, older adults constitute the group with the highest prevalence of T2DM and, at the same time, the most complex one for clinical management due to the high frequency of frailty, multimorbidity, and risk for hypoglycemia. (10) In older adults, hypoglycemia is associated with falls, cognitive decline, hospitalizations, cardiovascular events, and increased mortality. (11) Several studies have documented cases of potential overtreatment, demonstrating a notable incidence of hypoglycemia and its association with adverse events. (12–14) Glycated hemoglobin (HbA1c) is the gold standard for evaluating glycemic control, as it reflects average blood glucose levels over the previous 8–12 weeks. However, evidence about the optimal values in older adults remains limited, partly due to their historical underrepresentation in clinical trials and the growing need to tailor goals based on frailty, comorbidities, and risk for hypoglycemia. (15,16) Consequently, guidelines for the management of T2DM in this population (17) recommend tailored targets based on functional status, comorbidities, and life expectancy, proposing stricter targets (HbA1c < 7.5%) for independent individuals and more flexible values (≈8%) for frail older adults or those with cognitive impairment. (18,19) Beyond glycemic control, managing other key aspects of comprehensive care, particularly cardiovascular comorbidities, is imperative. Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in individuals with T2DM, with dyslipidemia being one of the most significant risk factors for its development. (20) Atherogenic dyslipidemia is common in these patients, characterized by elevated low-density lipoprotein cholesterol (LDL-C)—with a predominance of small, dense particles—increased

triglycerides (TG), and decreased high-density lipoprotein cholesterol (HDL-C). (21) Although reducing LDL-C remains the initial therapeutic goal, (22) there is growing evidence that measures such as non-HDL cholesterol (non-HDL-C) and apolipoprotein B (ApoB), as well as the TG/HDL-C ratio, may better predict cardiovascular risk than standard lipid parameters. (23) In our country, population aging—which, as previously noted, increases the burden of noncommunicable diseases and places a growing demand on healthcare systems—requires careful planning of strategies for the care of older adults. (24) Therefore, it is essential to understand the characteristics of this population, paying particular attention to prevalent diseases such as T2DM.

OBJECTIVE

The aim of this study was to describe the association between glycemic control, hypoglycemic drug therapy, and cardiovascular risk in older adults with T2DM managed at a medical center in the city of Rosario, Argentina.

METHODS

We conducted an observational descriptive study using conveniently anonymized data collected from patient laboratory records at the Policlínico PAMI I in Rosario.

We estimated a sample size of 350 patients for a 95% confidence level and a 5% margin of error. Data from patients presenting between January and December 2023 were included in the study.

The study included functionally independent patients of both sexes, ≥ 60 years, diagnosed with T2DM.

Statistical Analysis

Qualitative variables are presented as frequency and percentage; quantitative variables are presented as mean and standard deviation (SD) or median and interquartile range (IQR), depending on whether their distribution is normal or non-normal.

The variables analyzed included age, sex, BMI, associated comorbidities, hypoglycemic drug therapy, glycemic control (YES/NO), and plasma parameters including total cholesterol (TC), HDL-C, LDL-C, TG, fasting glucose (G0), and HbA1c.

The following indices were calculated: non-HDL-C (TC – HDL-C); Castelli I index (TC/HDL-C); Castelli II index (LDL-C/HDL-C); and the TG/HDL ratio.

Glycemic control was achieved when G0 levels were < 120 mg/dL and HbA1c levels were $< 7.5\%$. (25)

The lipid profile variables had missing values in 15% of cases. Because these variables were relevant to the objectives of the study, the missing data were handled using multiple imputation by fully conditional specification. Five imputed datasets were generated, using regression models appropriate for the type of variable and incorporating related clinical variables as predictors. Statistical analyses were performed by combining the estimates obtained from the imputed datasets, in accordance with Rubin's rules. (26)

Ethical considerations

The project was approved by the Ethics Committee of the School of Medical Sciences at the National University of Ro-

sario and endorsed by the authorities of Policlínico PAMI I in Rosario.

RESULTS

Data from 350 older adults diagnosed with T2DM were analyzed; 167 were women (47.7%), and 183 were men (52.3%).

Table 1 shows the values for plasma parameters and age, analyzed across the complete dataset (including both original and imputed data).

Mean BMI was 30.6 kg/m^2 ; 323 patients (92.3%) were in the overweight or obesity range ($\text{BMI} \geq 25 \text{ kg/m}^2$).

Mean G0 and HbA1c values were $142.1 \pm 45.0 \text{ mg/dL}$ and $7.2 \pm 1.7\%$, respectively. Based on the established criteria, 63.2% of patients achieved adequate glycemic control; the remaining 36.8% did not meet the proposed targets, and 15% had an $\text{HbA1c} \leq 6\%$.

Regarding the lipid profile, mean values were as follows: TC, $165.0 \pm 42.4 \text{ mg/dL}$; HDL-C, $51.2 \pm 13.3 \text{ mg/dL}$; LDL-C, $91.2 \pm 36.0 \text{ mg/dL}$; and TG, $136.3 \pm 74.0 \text{ mg/dL}$. The atherogenic indices calculated from these values are shown in Table 2, analyzed according to the level of glycemic control achieved.

The most common comorbidities were hypertension in 292 patients (83.4%), followed by dyslipidemia in 128 (36.6%), and cardiovascular disease, detected in 56 patients (16.0%). Two or more comorbidities were identified in 228 patients (65.1%), and only 25 (7.1%) patients had no associated comorbidities.

Regarding glucose-lowering drugs, Table 3 presents the frequency of use of each one as monotherapy or combination therapy. Metformin was the drug most commonly used ($n = 255$, 72.8%), with 51.0% ($n = 130$) receiving it as monotherapy. The most common combinations were metformin with sulfonylureas and/or dipeptidyl peptidase-4 (DPP-4) inhibitors. Cardioprotective antidiabetic drugs, such as GLP-1 receptor agonists and SGLT2 inhibitors, were used in 5.7% of all patients, always in combination therapy.

Table 1. Baseline characteristics ($n = 350$)

Variable	Mean $\pm$ SD
Age (years)	72.0 ± 7.7
BMI (kg/m^2)	30.6 ± 4.9
G ₀ (mg/dL)	142.1 ± 45.0
HbA1c (%)	7.2 ± 1.7
*TC (mg/dL)	165.0 ± 42.4
*HDL-C (mg/dL)	51.2 ± 13.3
*LDL-C (mg/dL)	91.2 ± 36.0
*TG (mg/dL)	136.3 ± 74.0

Note: *Values correspond to data obtained after multiple imputation to handle missing data; number of original values $n = 297$.

BMI: body mass index; G0: fasting blood glucose; HbA1c: glycated hemoglobin; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; TC: total cholesterol; TG: triglycerides

Table 2. Patient's distribution according to glycemic control and atherogenic indices

Atherogenic indices	Categories	Glycemic control			
		Adequate (n = 221)		Poor (n = 129)	
non-HDL-C (p=0,297) *	Normal (≤ 130 mg/dl)	161	(72.8%)	87	(67.4%)
	Abnormal (>130 mg/dl)	60	(27.2%)	42	(32.6%)
Castelli index I (p=1,000)*	Normal (M: < 3.5 ; F: < 3)	122	(55.2%)	72	(55.8%)
	Abnormal (M: ≥ 3.5 ; F: ≥ 3)	99	(44.8%)	57	(44.2%)
Castelli index II p=0,312) *	Normal (M: < 2.5 ; F: < 2)	164	(74.2%)	88	(68.2%)
	Abnormal (M: ≥ 2.5 ; F: ≥ 2)	57	(25.8%)	41	(31.8%)
Atherogenic index (p=0,276) *	Normal (< 3)	147	(66.5%)	76	(58.9%)
	Abnormal (≥ 3)	74	(33.5%)	53	(41.1%)

Note: Data are expressed as percentages by column. * Fisher's exact test was applied for each index.
F: female; M: male

DISCUSSION

The well-established trend of population aging in Argentina—which, according to ECLAC and INDEC, will continue to increase the burden of chronic diseases—justifies conducting studies such as this one, focused on the older adult population. (3,4)

Within the context of the demographic and risk factors analyzed, the high prevalence of overweight or obesity detected in the sample is consistent with the global trend reported by the IDF Atlas, which identifies obesity as one of the primary drivers of the T2DM epidemic. (8) Although excess weight has traditionally been the key risk factor, it is worth noting that, as Suastika et al. (6) concluded, in older adults, age is a strong independent factor, primarily due to reduced insulin sensitivity.

Our study found adequate glycemic control in 63.2% of patients, with a mean HbA1c value of 7.2%. These values are in line with the recommendations of the Argentine Society of Diabetes and the ADA, which suggest HbA1c targets below 7.5% for functionally independent older adults. (27,28) However, this apparent therapeutic success should be interpreted with caution, because 15.0% of the entire cohort had HbA1c levels $\leq 6.0\%$, which may indicate potential overtreatment. Studies in similar populations, such as those by Lega in Ontario and Mata-Cases in Catalonia, have shown that intensive glycemic control (HbA1c $< 7\%$) in older adults—especially with the use of insulin or sulfonylureas—is associated with an almost 50% increase in the risk of emergency department visits, hospitalizations, and death due to episodes of hypoglycemia. (13,14) Given that 33.1% of our cohort uses combination therapy with sulfonylureas or DPP-4 inhibitors, it would be advisable to emphasize the importance of close monitoring in these cases.

Regarding the lipid profile, mean plasma lipid levels were within acceptable ranges. However, analysis of atherogenic indices revealed a significant residual risk. (29,30) The literature highlights that the TG/HDL-C ratio is a better predictor of cardiovascular risk

Table 3. Pharmacological groups used

Pharmacological group	As monotherapy or combination therapy	
	n	%
Metformin	72.8	72.8
Sulfonylureas	25.1	25.1
DPP-4 inhibitors	8.0	8.0
SGLT2i	5.1	5.1
Insulin	2.0	2.0
Thiazolidinediones	0.6	0.6
GLP-1 RAs	0.6	0.6

Note: Percentages were calculated based on the total number of patients (n=350). The sum of the percentages exceeds 100% because some patients received more than one drug as part of combination therapy.
DPP-4: dipeptidyl peptidase-4; GLP-1 RAs: glucagon-like peptide-1 receptor agonists; SGLT2i: sodium-glucose cotransporter-2 inhibitors

and insulin resistance than LDL-C alone, especially for identifying the presence of small, dense LDL-C particles, which are highly atherogenic. (31–34) In our study, the persistence of abnormal lipid indices even in patients with good glycemic control suggests that metabolic management must go beyond blood glucose levels to address atherogenic dyslipidemia with a comprehensive approach.

A notable finding in our study regarding pharmacological treatment is the low use of cardioprotective agents (GLP-1 receptor agonists and SGLT2 inhibitors) prescribed to only 5.7% of patients. This figure is striking given the presence of significant cardiovascular risk factors, such as age, T2DM, and the high prevalence of hypertension in the sample. Current ADA and ESC/EAS guidelines (22,28) emphasize that these agents should be considered essential for managing patients at high cardiovascular risk, regardless of the HbA1c target achieved, due to their proven benefit in reducing major events. In turn, another cardiovascular risk factor—the presence of overweight

or obesity (92.3% in our sample)—should guide the choice toward medications that not only control glucose levels but also promote weight loss, because this is associated with better glycemic control. GLP-1 RAs and SGLT2i also have beneficial effects in this regard. (28)

In line with our results, the Argentine Society of Cardiology underscores the use of cardioprotective drugs. (35) A document from the Argentine Federation of Cardiology (36) notes their low usage rate—less than 10% of cases—a finding consistent with other sources. (37,38) Therapeutic inertia and high costs limit the adoption of these therapies. To avoid therapeutic inertia and ensure optimal control, the Argentine Society of Diabetes (SAD) recommends periodic treatment reassessment every 3–6 months. In terms of costs, the recent introduction of domestically manufactured drugs into the market—compared with imported alternatives—will facilitate access to a therapeutic option previously restricted by financial constraints.

Strengths and limitations. This study provides data on a cohort of older adults with T2DM in Argentina, a population that is often underrepresented in large clinical trials. Furthermore, the use of multiple imputation to handle missing data contributes to the robustness of the results. Among the limitations, the descriptive nature of our study prevents establishing cause-and-effect relationships. Furthermore, because the cohort was from a single center in Rosario city, caution is warranted when extrapolating the findings nationwide.

In addition, the patients were enrolled in the PAMI health insurance system, whose policies regarding access to and coverage for certain glucose-lowering drugs with proven cardiovascular benefits—such as GLP-1 receptor agonists and SGLT2 inhibitors—may have influenced the low utilization rates observed for these medications.

In conclusion, while most patients in this cohort of older adults with T2DM achieved traditional glycemic control targets, utilization of glucose-lowering drugs with proven cardiovascular benefits was low, and a significant proportion of patients presented potential overtreatment. More than half of the patients with adequate glycemic control had atherogenic indices consistent with a high residual cardiovascular risk, indicating that glycemic target achievement alone does not ensure cardiovascular risk reduction. These findings highlight the need to integrate atherogenic indices into routine cardiovascular risk assessment and support the need for therapeutic strategies that simultaneously address glycemic control and residual cardiovascular risk reduction.

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Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web).

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