


 Isabela Rosendo Mendonça¹
 Alexandre Bitencourt Rosendo²
 Bruna Becker da Silva³
 Betine Pinto Moehlecke Iser³

¹ Universidade do Sul de Santa Catarina, Curso de Medicina. Tubarão, SC, Brasil.

² Ciclos Medicina, Clínica. Tubarão, SC, Brasil.

³ Universidade do Sul de Santa Catarina, Programa de Pós-Graduação em Ciências da Saúde. Tubarão, SC, Brasil.

Correspondence
Betine Pinto Moehlecke Iser
betinee@gmail.com

Association between therapeutic adherence and glycemic control in patients with type 2 diabetes mellitus

Associação entre a adesão terapêutica e o controle glicêmico de pacientes com diabetes mellitus tipo 2

Abstract

Introduction: Treatment adherence in diabetes mellitus is essential for metabolic control, complication prevention, quality of life improvement and maintenance. **Objective:** To assess the association between adherence with pharmacological treatment and glycemic control in patients with type 2 diabetes and investigate factors associated with these conditions. **Method:** This is a cross-sectional study with patients ≥ 18 years old with type 2 diabetes mellitus, treated at a private endocrinology service, using oral antidiabetics for at least 6 months and with a glycated hemoglobin (HbA1c) measurement for a maximum of 12 months. The MMAS-8 (Morisky Medication Adherence Scale) and a questionnaire with sociodemographic and clinical data were used. Results presented as prevalence ratio (PR) and 95% confidence interval (CI), adjusted by logistic regression using the enter method. The level of statistical significance adopted was 5%. **Results:** A total of 134 patients participated in the study, with a mean age of 56.7 ± 12.9 years, 58.2% of whom were women. Therapeutic adherence was demonstrated by 78.4% of patients, with a positive association with education and a negative association with age and time since diagnosis. Glycemic control was verified by 68.7%, with no statistically significant difference in relation to sex, age, race, education and time since diagnosis. Among patients considered adherent, 77.1% had adequate glycemic control, while among patients considered non-adherent, 37.9% were considered controlled ($p < 0.001$). **Conclusion:** Pharmacological treatment adherence was associated with glycemic control in patients with type 2 diabetes followed up in a private endocrinology office.

Keywords: Type 2 Diabetes Mellitus. Medication Adherence. Glycated Hemoglobin. Glycemic Control.

Resumo

Introdução: A adesão ao tratamento no diabetes mellitus é fundamental para o controle metabólico, prevenção de complicações, melhoria e manutenção da qualidade de vida. **Objetivo:** Avaliar a associação entre a adesão ao tratamento farmacológico e o controle glicêmico de pacientes diabéticos tipo 2 e investigar fatores associados a essas condições. **Método:** Estudo transversal com pacientes ≥ 18 anos com diabetes mellitus tipo 2, atendidos em um serviço privado de endocrinologia, em uso de antidiabéticos orais há pelo menos 6 meses e com dosagem de hemoglobina glicada (HbA1c) de no máximo 12 meses. Foram utilizados a MMAS-8 (Morisky Medication Adherence Scale) e um questionário com dados sociodemográficos e clínicos. Resultados apresentados em razão de prevalência (RP) e intervalo de confiança (IC) 95%, ajustados por regressão logística pelo método enter. O nível de significância estatística adotado foi de 5%. **Resultados:** Participaram do estudo 134 pacientes, com

média de $56,7 \pm 12,9$ anos, sendo 58,2% mulheres. A adesão terapêutica foi demonstrada por 78,4% dos pacientes, havendo associação positiva com a escolaridade e negativa em relação à idade e ao tempo de diagnóstico. O controle glicêmico foi verificado por 68,7%, não havendo diferença estatisticamente significativa em relação a sexo, idade, raça, escolaridade e tempo de diagnóstico. Entre os pacientes considerados aderentes, 77,1% apresentaram controle adequado da glicemia, enquanto entre pacientes considerados não aderentes, 37,9% foram considerados controlados ($p < 0,001$). **Conclusão:** A adesão ao tratamento farmacológico esteve associada ao controle glicêmico em pacientes com diabetes tipo 2, acompanhados em consultório privado de endocrinologia.

Palavras-chave: Diabetes Mellitus Tipo 2. Adesão à Medicação. Hemoglobina Glicada. Controle glicêmico.

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disease characterized by high blood glucose levels, resulting from deficiency in insulin secretion and/or action, or both mechanisms, which lead to changes in the metabolism of carbohydrates, lipids, proteins and electrolytes.^{1,2} Type 2 diabetes mellitus (T2DM) is the most common type and is often associated with obesity and aging. Its onset is insidious and is characterized by insulin resistance and partial deficiency of insulin secretion by pancreatic β cells, established by hyperglycemia identification. Fasting plasma glucose ≥ 126 mg/dl, blood glucose two hours after an overload of 75 g of anhydrous glucose (TOTG) ≥ 200 mg/dl, glycated hemoglobin (HbA1c) $\geq 6.5\%$ are recommended as diagnostic criteria for T2DM. Two altered tests are required to confirm diagnosis.³

Regarding global prevalence, estimates from 2021 indicated that T2DM would affect around 16% of the world population, standardized for the age range of 20 to 79 years. According to the latest publication from the International Diabetes Federation, around 537 million people have DM worldwide, and between 2019 and 2021, there was an increase of 74 million cases, corresponding to an incidence of 16%. For the coming years, the projection is for 643 million people with T2DM in 2030 and 784 million people with T2DM in 2045.²

The population of people affected by the disease in Brazil is estimated at 16.8 million, and the country ranks 5th worldwide.² Between 2020 and 2022, according to the *Vigilância de Fatores de Risco e Proteção para Doenças Crônicas por Inquérito Telefônico* (MGITEL, Surveillance of Risk and Protective Factors for Chronic Diseases by Telephone Survey), carried out by the Ministry of Health, DM prevalence increased from 8.2% to 9.1% – an increase of 11.47% in the period.⁴

T2DM natural history is marked by the appearance of chronic complications, generally classified as microvascular – retinopathy, nephropathy and neuropathy – and macrovascular – coronary artery disease, cerebrovascular and peripheral vascular disease. All are responsible for significant morbidity and mortality, with rates of cardiovascular and renal mortality, blindness, limb amputation and loss of function and quality of life higher than those found in individuals without DM.⁵

As T2DM is an evolutionary disease, positive changes in lifestyle, such as food and physical activity, are of fundamental importance in achieving treatment objectives. However, over time, all patients require pharmacological treatment, as pancreatic beta cells tend to progress to a state of partial or total failure over the years.⁵

In people with T2DM, treatment adherence is essential for metabolic control, complication prevention, quality of life improvement and maintenance. According to the World Health Organization (WHO), adherence is defined as adequate adherence to medical treatment and prescribed care. According to the WHO, only 50% of people with chronic diseases adhere to treatment in developed countries, whereas, in developing countries, this problem has an even greater proportion and impact, considering the scarcity of resources and the difficulty in accessing health services.⁶

Non-adherence to pharmacological treatment is one of the main causes of worsening of the disease in people with DM, due to failure to achieve adequate glycemic control and, as a result, decreased life expectancy and quality of life.⁷

Using tools, such as the Morisky-Green test,⁸ allows non-adherent patients to be identified to direct actions, mainly educational, that promote an improvement in adherence and disease control through the development of self-care skills. With the increasing DM prevalence, it is important to research factors that interfere with adherence to DM pharmacological treatment.⁹

Considering the above, this study aimed to assess the association between adherence to pharmacological treatment and glycemic control in patients with T2DM as well as to investigate other factors associated with these conditions.

METHOD

This is a cross-sectional study, carried out at a private endocrinology service in a municipality in southern Santa Catarina. The sample was for convenience, starting from all patients followed by the service at the time of the study, estimating 120 patients. Individuals with T2DM, of both sexes, aged 18 years and older, who had been using oral antidiabetics for at least 6 months and who had glycated

hemoglobin (HbA1c) levels for a maximum of 12 months prior to the application of the questionnaires, were included. Patients with cognitive difficulties that limited understanding of the study and responses to the questionnaires were excluded.

After checking the list of patients receiving care at the service, they were invited to participate in the research via telephone call from July to September 2020, and were advised on the objectives of the study. Those who confirmed that they met the inclusion criteria and agreed to participate in the study received via WhatsApp a link containing an online Informed Consent Form and data collection questionnaire in Google Forms. Contact data with patients were collected from the place of care and used exclusively for the research. Patients were completely free to participate voluntarily by accessing the form link, without any link between their participation in the research and the care received.

Two instruments were applied to research participants. The first was a questionnaire previously structured by the authors of the study that investigated sociodemographic data (sex (male/female); skin color (white/black); age (continuous and categorized as 30 to 59 years/ ≥ 60 years); and education level (illiterate/incomplete elementary school/complete elementary school/incomplete medical education/complete high school/incomplete higher education/complete higher education/graduate education, further categorized into up to high school; higher education) and clinical data (time of diagnosis recorded in years and dichotomized into ≤ 6 years and > 6 years, presence of chronic complications of DM, comorbidities and types of oral antidiabetics and insulin used). Upon authorization, patients' medical records were checked to identify additional information about test results.

The second instrument was the Morisky-Green Therapeutic Adherence Scale⁷ (MMAS-8), already validated and adapted for use in Brazil. MMAS-8 contains eight questions, the first seven of which require a dichotomous answer (yes/no) and the last question uses a five-point Likert scale.⁸ Therapeutic adherence degree was determined according to the score resulting from the sum of all correct answers, i.e., negative for inappropriate behaviors, being considered high adherence (eight points), medium adherence (six to seven points) and low adherence (< 6 points). In the present study, for comparison purposes, variables were dichotomized, with patients with a score equal to or greater than six on the MMAS-8 considered adherent.⁸

Glycemic control, the study's primary outcome of interest, was determined based on the last HbA1c value in the 12-month period prior to the application of the questionnaires. Adult patients were considered controlled when HbA1c was $< 7\%$, in older adults without comorbidities, when $< 7.5\%$, and in older adults with comorbidities other than T2DM, when $< 8\%$.¹⁰

Data were organized in a Microsoft Excel spreadsheet and analyzed using SPSS version 21.0. Quantitative variables were described using measures of central tendency and data dispersion (mean \pm standard deviation). Qualitative variables were described using absolute and percentage frequencies. Differences in proportions were tested using the chi-square test and differences in means using Student's t-test or ANOVA, or non-parametric equivalents, depending on data adequacy. Binary analysis results were presented as prevalence ratio (PR) and 95% confidence interval (CI).

Considering the association of therapeutic adherence with glycemic control as the main purpose of the study, variables involved in this relationship were considered in an adjusted model. Therefore, variables with a p-value < 0.20 in bivariate analysis were submitted to multivariate analysis using logistic regression using the enter method in chunks (age, education, time since diagnosis, comorbidity, insulin use, complications of T2DM; and for the glycemic control outcome, therapeutic adherence), with the results expressed as Odds Ratios (OR) and 95% CI. The level of statistical significance adopted was 5%.

The project was approved by the Research Ethics Committee of the *Universidade do Sul de Santa Catarina*, under Opinion 4,165,529 of July 2020. All participants signed the Informed Consent Form, as recommended by Resolution 466/2012 of the Brazilian National Council of Health.

RESULTS

The sample consisted of 134 patients, aged between 31 and 86 years, mean of 56.68 ± 12.90 years, of which 58.2% were women. Regarding skin color, 96.3% are white. Regarding education analysis, 91.8% have at least completed high school. Table 1 presents the sample sociodemographic characteristics. The mean time since diagnosis of T2DM was 8.2 ± 6.62 years.

Table 1. Epidemiological profile of patients with type 2 diabetes participating in the study, Tubarão - SC, 2020 (N=134).

	n	%
Sex		
Male	56	41.8
Female	78	58.2
Skin color		
White	129	96.3
Black	05	3.7
Education		
Illiterate	0	0
Incomplete elementary school	2	1.5
Complete elementary school	9	6.7
Incomplete high school	8	6
Complete high school	37	27.6
Incomplete higher education	25	18.7
Complete higher education	48	35.8
Graduate degree	5	3.7
Age group		
30 – 59 years	73	54.4
≥ 60 years	61	45.6

Table 2 describes the characteristics of pharmacological treatment (use and types of oral antidiabetics and insulin/analogues) of patients with T2DM. The medication most frequently used by patients was metformin, either alone or in combination with another hypoglycemic agent, present in the therapeutic regimen of 126 patients. In addition to oral medication, 26.9% reported using insulin. Among insulin users, the most used by patients was NPH, used by 50% of patients in this group, followed by glargine, used by 33.3% of these patients.

Table 2. Types of medications used by patients with type 2 diabetes participating in the study, Tubarão - SC, 2020 (N=134)

	n	%
Type of oral antidiabetic drug		
Dapagliflozin	2	1.5
Glibenclamide	6	4.5
Metformin	94	70.1
Metformin/dapagliflozin	8	6
Metformin/glibenclamide	20	14.9
Metformin/gliclazide	4	2.9
Type of insulin (n=36)		
Degludec	5	13.9
Glargine	10	27.8
NPH	11	30.5
Degludec/regular	1	2.8
Glargine/regular	2	5.6
NPH/regular	7	19.4

Regarding data from control laboratory tests, 56.0% of patients had fasting blood glucose levels greater than 130 mg/dl, with a mean of 143.31 mg/dl (SD ± 40.59). Regarding glycosylated hemoglobin levels in the last 12 months, 52.2% had values less than or equal to 7%.

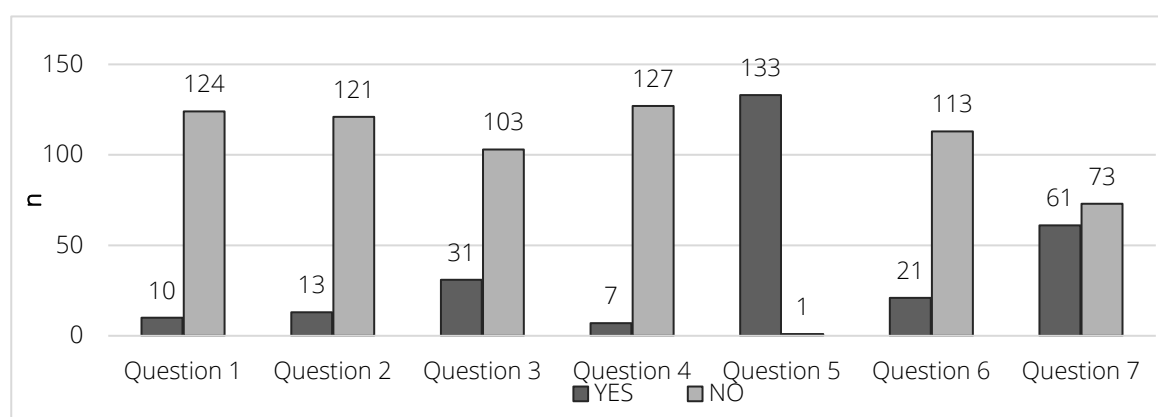
Of the total number of patients studied, 14.9% reported the presence of complications of T2DM. Table 3 describes chronic complications (nephropathy, neuropathy and retinopathy) resulting from T2DM in patients participating in the present study and their other comorbidities. Most (67.2%) patients reported having another comorbidity in addition to DM, with hypertension being the most prevalent, affecting 41% patients and equivalent to 47.8% of the comorbidities mentioned.

Table 3. Chronic complications resulting from diabetes mellitus and other comorbidities presented by patients participating in the study, Tubarão - SC, 2020 (N=134).

	n	%
Chronic complications (n=20)		
Nephropathy	4	20
Neuropathy	2	10
Retinopathy	7	35
Nephropathy/retinopathy	6	30
Neuropathy/retinopathy	1	5
Comorbidities (n=90)		
Anxiety	10	8.7
Asthma	3	2.6
Comorbidities (n=90)		
Bronchitis	2	1.7
Prostate cancer	1	0.9
Depression	13	11.3
Dyslipidemia	11	9.5
Diverticulitis	1	0.9
GERD	1	0.9
Fibromyalgia	1	0.9
Benign prostatic hyperplasia	1	0.9
Hypertension	55	47.8
Hypothyroidism	10	8.7
Osteoporosis	2	1.7
Parkinson's	1	0.9
Allergic rhinitis	3	2.6

Morisky-Green medication adherence test results indicated that 21.8% patients reported non-adherence to medication, while 78.4% reported adherence. Among the reasons that lead to non-adherence to medication, the most common was feeling uncomfortable about correctly following treatment regimen for T2DM (45.5%), as detailed in Figure 1.

Figure 1. Patients' responses to the first seven dichotomous questions of the Morisky-Green Adherence Scale (MMAS-8), Tubarão - SC, 2020



Caption: Question 1: Do you sometimes forget to take your medicine?; Question 2: Was there a day when you did not take your medicine?; Question 3: Have you stopped taking it or reduced the dose without telling your doctor?; Question

4: When you travel or go out, do you forget to take your medicines?; Question 5: Did you take your medications yesterday?; Question 6: When you feel your diabetes is under control, do you sometimes stop taking the medication?; Question 7: Have you ever felt uncomfortable following your treatment correctly?

When relating patients' levels of therapeutic adherence to their sociodemographic variables, it was found that the mean age of those with adherence was 54.0 ± 12.3 years and of those without adherence was 66.3 ± 9.8 years ($p < 0.001$). Therapeutic adherence was verified in 91.8% of adults (30 to 59 years old) and in 62.3% of older adults (≥ 60 years old) ($p < 0.001$). There was no significant difference in adherence degree between men and women and between whites and non-whites. Regarding education, it was observed that patients with less education (up to complete high school) showed lower adherence to medication treatment (60.7%) than those with a higher level of education (complete or incomplete higher education or graduates), of which 91.0% were considered adherent. Table 4 describes the association between therapeutic adherence and other characteristics studied.

Table 4. Relationship between therapeutic adherence and glycemic control and sociodemographic variables and other characteristics arising from diabetes, Tubarão - SC, 2020

Variables	Treatment adherence			Glycemic control		
	Yes %	No %	PR (95%CI)	Yes %	No %	PR (95%CI)
Sex						
Female	82.1	17.9	1.12 (0.93-1.35)	74.4	25.6	1.23 (0.95-1.57)
Male	73.2	26.8		60.7	39.3	
Age (years)						
30-59	91.8	8.2	1.47 (1.20-1.81)*	69.9	30.1	1.04 (0.83-1.31)
≥ 60	62.3	37.7		67.2	32.8	
Education						
Up to high school	60.7	39.3	0.67 (0.53-0.83)*	62.5	37.5	0.86 (0.67-1.09)
Higher education	91.0	9.0		73.1	26.9	
Skin color						
White	78.3	21.7	0.98 (0.63-1.53)	68.2	31.8	0.85 (0.54-1.34)
Non-white	80.0	20.0		80.0	20.0	
Time since diagnosis						
≤ 6 years	87.3	12.7	1.28 (1.06-1.55)*	71.8	28.2	1.10 (0.88-1.39)
> 6 years	68.3	31.7		65.1	34.9	
Use of insulin						
Yes	52.8	47.2	0.60 (0.44-0.83)*	52.8	47.2	0.71 (0.51-0.99)*
No	87.8	12.2		74.5	25.5	

When associating glycemic control with sociodemographic variables, it was noticed that glycemic control decreased with advancing age, being 85.7% between 30-49 years old, 62.9% between 50-69 years old and 54.5% of patients aged 70 or over ($p = 0.012$). However, there was no significant difference in DM control between adults and older adults (Table 4). In relation to sex, race and education, there was also no statistically significant difference, as detailed in Table 4.

Regarding time since diagnosis, patients with the most recent disease showed greater adherence to drug treatment (87.3%) than those with more than six years of DM (68.3%). Regarding glycemic control, time since diagnosis did not significantly interfere (Table 4). Patients who reported complications of DM and other comorbidities were those with a longer time since diagnosis: the mean years of diagnosis for those with complications was 14.4 ± 7.92 years, while for those

without complications, it was 7.1 ± 5.74 years ($p < 0.001$). In patients who had comorbidities other than T2DM, the mean time since diagnosis was 9.4 ± 7.35 years, longer than those without comorbidities (average 5.7 ± 3.77 years; $p = 0.002$). Time since diagnosis was also longer in patients with non-adherence to medication (13.1 ± 10.06 years) – compared to the mean of 6.9 ± 4.49 years in those with good adherence ($p < 0.001$).

Patients who reported using insulin had 40% less treatment adherence and 29% less disease control. The occurrence of complications of DM was also associated with low adherence and worse control, with patients with complications having 65% lower adherence and 60% lower glycemic control (Table 4).

Among patients who adhered to treatment, 77.1% had adequate glycemic control. On the other hand, of patients without medication adherence, only 37.9% could be considered as adequately controlled ($p < 0.001$), thus demonstrating that adequate medication treatment can increase glycemic control by up to 2 times ($PR = 2.03$ 95%CI 1.3-3.3). It was also found that adherence reduces the risk of complications by 88% ($PR = 0.12$; 95% CI 0.05-0.28) and that glycemic control reduces the occurrence of complications of DM by 80% ($PR = 0.20$; 95%CI 0.08-0.47).

When exploring the relationship between therapeutic adherence and glycemic control according to time since DM diagnosis, despite the fact that, regardless of the time of diagnosis, those who are most adherent are more controlled, differences in glycemic control between adherent and non-adherent patients were more evident in those with longer DM ($> six$ years). This demonstrates that adherence to therapeutic regimen is even more important for adequate glycemic control the longer the illness lasts (Table 4).

Considering the different factors associated with therapeutic adherence and, consequently, glycemic control, the multivariate model included age, education, time since diagnosis, insulin use, presence of comorbidities and complications of T2DM. It was found that having complications of DM has a negative association with adherence ($OR = 0.11$; 95% CI 0.028-0.42) and that therapeutic adherence increases disease control by 3.5 times ($OR = 3.46$; 95%CI 1.18-10.20), regardless of age, education, time since diagnosis, presence of comorbidity, use of insulin and complications of disease (data not shown in table).

DISCUSSION

In the present study, it was possible to observe that adherence to pharmacological treatment of patients with T2DM is influenced by factors such as age, education, time since diagnosis and presence of comorbidities and complications of DM. Adherence, in turn, was associated with glycemic control in patients with T2DM participating in the study followed up in a private endocrinology service.

A higher proportion of women with DM was observed. Carvalho et al.¹¹ and Arrelias et al.,¹⁰ in cross-sectional studies with patients with DM, also found a higher proportion of women with T2DM. The higher frequency of women with T2DM may be associated with the fact that they tend to seek health care services more frequently than men.¹² We observed a higher frequency of white skin color, and most participants were between 30 and 59 years of age, data that corroborates other studies.¹³⁻¹⁵

Studies have also shown a significant increase in T2DM in individuals aged 65 and older,¹⁶ since, with the population's greater life expectancy, aging leads to a greater chronic non-communicable disease prevalence.^{17,18} It should also be noted that the demand for health services increases with the population's aging, combined with decreased infectious and parasitic disease incidence and increased chronic diseases such as T2DM.¹⁸

With regard to glycemic control, older patients were those who had the worst control, which demonstrates the difficulty of adhering to treatment and the need for reinforcement of a T2DM education program in the study unit. Furthermore, the literature tells us that older adults have difficulty adhering to treatment, which may be related to the

difficulty in adapting to changing lifestyle habits, such as use of oral medications, insulin administration, self-monitoring of blood glucose levels, physical activity and diet.¹⁹

Individuals with more than eight years of education were the majority among T2DM diagnoses, opposing data obtained in the literature.^{13,16,17,20} This discrepancy can be explained by the fact that the study population is made up of patients from a private endocrinology service who may have better financial conditions and, therefore, a greater probability of having education levels above the average found in the literature. The importance of analyzing education level is due to the fact that the educational level can make access to information difficult and bring fewer opportunities for learning in health care, thus making it difficult to correctly carry out the prescribed therapy and, consequently, glycemic control.

Most patients used only one medication for pharmacological treatment, with metformin being the most frequently mentioned drug in patients' therapeutic regimen, corroborating Silva et al.²¹ and Gomes et al.²² Metformin is known to have satisfactory effects on HbA1c, considering its advantage in glycemic control, cardiovascular event reduction, lipid profile improvement and weight reduction.⁵

Given the progressive nature of the disease or prolonged use of a first medication, there may be a need for a second line of pharmacological treatment. On average, 50% of people who achieve glycemic control with monotherapy require the combination of another medication after two years of treatment.²³ The drug most associated with metformin in this study was glibenclamide, which is in line with Ministry of Health data, which states that the second oral hypoglycemic agent of choice for association with metformin is from the sulfonylurea class, which increase insulin secretion, with glibenclamide being the most commonly prescribed and made available by the *Sistema Único de Saúde* (SUS, Brazilian Health System) as well as gliclazide.²⁴

However, the lack of metabolic control after using these associated medications often requires a third line of treatment. The most common, particularly in people with longer duration of T2DM, is addition of basal insulin, or human NPH, or one of the long-acting insulin analogs to oral agent regimens.²³ This fact was evidenced by this study as well as the fact that patients who use insulin showed less adherence and disease control.

In relation to glycemic control, HbA1C levels below 7% are prioritized. However, HbA1C goals were individualized taking into account age group and presence of chronic complications or comorbidities, since, according to the American Diabetes Association (ADA), individuals who possess such characteristics may be targeted for less stringent controls of up to 8%.¹ In the present study, most patients were considered to have adequate control, with a value close to that presented in the study by Machado et al.,¹⁴ which reported a percentage of 68.9%. Among the age groups of 30-49 years, 50-69 years and ≥ 70 years, it was observed that glycemic control was influenced by age, with a difference from 85.7% of patients controlled in the younger group to 54.5% in the older group. This fact corroborates studies that state that age is a complicating factor in achieving good glycemic control, mainly due to difficulties in understanding information about the disease and applying these guidelines in self-care, resulting from progressive cognitive and functional deficit over the years or increased dependence degree to carry out actions such as taking medications.²⁵

Studies highlight the close relationship between accurate glycemic control, evidenced by HbA1C, and prevention of onset or evolution of chronic complications of DM. The results of the UKPDS²⁶ study showed that the microvascular complications of DM are reduced when there is good glycemic control, as demonstrated in the present study, in which patients considered adequately controlled reported 80% fewer complications than those with poor glycemic control.

Among the chronic microvascular complications of DM, diabetic retinopathy and nephropathy were the most prevalent, especially in those patients with a longer diagnosis period. Retinopathy is the most frequent cause of new cases of blindness among adults aged between 20 and 74 years of age, with a prevalence of 60% in patients with T2DM with more than 20 years of disease.²⁷ In relation to nephropathy, DM is considered the most relevant cause of kidney disease, accounting for the majority of people enrolled in dialysis programs.²⁸

Regarding associated comorbidities, hypertension was the most cited by study participants, followed by depression and dyslipidemia. This profile corroborates data from the literature that demonstrate that most individuals with T2DM tend to lack blood pressure and lipid control.²⁹ Hypertension is approximately twice as common among individuals with DM when compared to the general population, being present in 50% of patients at the time of diagnosis of T2DM.¹

Depression and anxiety were other comorbidities highlighted in this study. The association between depression and DM, verified in previous studies,^{30,31} raises concern due to its possible deleterious effect on DM treatment, since depressive symptoms can impair treatment maintenance, worsen glycemic control, and increase the risk of complications.³²

The percentage of patients considered to have good therapeutic adherence (with an MMAS-8 score \geq six) in this study was in agreement with other studies.^{10,11,26} Analyzing the responses obtained, in order to find possible causes of non-adherence, the most relevant factor described by patients was discomfort, i.e., did they ever feel uncomfortable following their DM treatment regimens correctly, which may be related to the need to follow medication use times and other factors that influence daily routine, such as having to follow a diet prescribed by a nutritionist, in some cases counting carbohydrates, in addition to having to practice physical exercise to better control the disease.

Regarding the factors associated with non-adherence, the present study did not show statistical differences between men and women, in line with what some studies say.^{9,25} Regarding age group, older adults were less adherent than adults, in line with data from the literature^{32,33} that consider age to be one of the barriers to treatment adherence, mainly due to cognitive and functional changes that progress with age, such as forgetfulness and visual problems, which can interfere with the ability to understand information about the disease, thus generating a deficit in self-care.^{34,35}

Therapeutic adherence was also lower among patients with less education, in accordance with national data.³⁶ It is inferred, therefore, that low education can make learning difficult, since, as the complexity of drug therapy for DM increases, patients need more complex cognitive skills to understand the drug treatment instituted and adhere to it.³²

Regarding time since diagnosis, it was observed that patients with the disease for a shorter period of time had a higher rate of treatment adherence. This inverse relationship between time since DM diagnosis and patients' adherence to drug therapy, already reported by the WHO,⁶ is concerning, given that the risks of chronic complications tend to increase with disease duration.³⁷

Following this line, in the present research, participants with lower adherence were also those who had a higher frequency of chronic complications, since good glycemic control is associated with complication prevention. This situation can be explained by the fact that patients adhere only to a very limited extent to therapeutic measures proposed by health professionals.¹⁷

Furthermore, low adherence is also associated with inadequate glycemic control, greater use of health resources, higher medical costs and markedly higher mortality rates.^{38,39} Regarding the relationship between therapeutic adherence and HbA1C, it was observed in this research that adequately adherent patients achieved glycemic control twice as high as that obtained by patients considered non-adherent, data consistent with the literature.⁴⁰

As limitations of this work, as it is a cross-sectional study, causality cannot be inferred in the associations found, and special caution must be taken when interpreting the relationships between occurrence of chronic complications of DM with therapeutic adherence and glycemic control. Furthermore, one can consider the fact that the sample studied is different, as it is being monitored in a private practice, and the level of adherence and control may not reflect the reality of a more heterogeneous population in socioeconomic terms and access to health care. On the other hand, this may also be a differentiator of this study, as it indicates the level of adherence of patients undergoing routine follow-up by the same specialist physician, a situation in which better adherence and disease control are expected.

Summing up, non-adherence to prescribed medication therapy can compromise treatment effectiveness, reducing or not producing the necessary clinical benefits, with direct consequences for patients' health.⁴¹ Although DM naturally has a prolonged course, its evolution can be accelerated by lack of adherence to prescribed treatment. For patients with chronic illness, failure to properly follow or abandon prescriptions leads to an increase in the number of hospital admissions, decreased effectiveness of pharmacological therapy, development of tolerance, increased treatment costs and loss of quality of life.⁵

Given the results evidenced in the present study, it is possible to understand the factors that lead the population with T2DM to non-treatment adherence. Thus, it becomes possible to intervene in order to increase effective participation in DM treatment in the population described, improving these patients' quality of life as well as reducing public spending. Furthermore, with these data it is possible to contribute to the establishment of local public health policies, reducing the morbidity rate of this disease.

CONCLUSION

We highlighted that, despite being monitored by a private endocrinology service, treatment adherence was average, influenced by factors such as age, education, time since diagnosis and presence of comorbidities and complications of DM. Adherence was associated with patients' glycemic control. This data may reflect that the strategies used for health education practices have been ineffective, as the low level of knowledge can influence reactions to coping with T2DM.

Thus, with a better understanding of these factors, it is possible to improve the strategies offered in care centers for people with T2DM, in addition to providing the basis for new ways of offering health care and improving public health policies for care for this population..

REFERENCES

1. American Diabetes Association. Standards of Medical Care in Diabetes [Internet]. Di-abetesCare. 2017 [Acesso em 08 de agosto de 2022]. Disponível em: http://care.diabetesjournals.org/content/diacare/suppl/2016/12/15/40.Supplement_1.DC1/DC_40_S1_final.pdf
2. International Diabetes Federation. IDF - Diabetes Atlas Ten edition 2021. 2021. [Acesso em 01 de abril de 2023]. Disponível em: <https://diabetesatlas.org/atlas/tenth-edition/>
3. Cobas R, Rodacki M, Giacaglia L, Calliari L, Noronha R, Valerio C, et al. Diagnóstico do diabetes e rastreamento do diabetes tipo 2. Diretriz Oficial da Sociedade Brasileira de Diabetes. 2022: 1-23. <https://doi.org/10.29327/557753.2022-2>
4. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. VIGITEL 2021: Vigilância de Fatores de Risco e Proteção para Doenças Crônicas em Inquérito Telefônico. Brasília: Ministério da Saúde; 2022. [Acesso em 01 de abril de 2023]. Disponível em: <https://www.gov.br/saude/pt-br/centrais-de-conteudo/publicacoes/svsa/vigitel/vigitel-brasil-2021-estimativas-sobre-frequencia-e-distribuicao-sociodemografica-de-fatores-de-risco-e-protecao-para-doencas-cronicas>
5. Brasil. Ministério da Saúde. Secretaria de Atenção à Saúde. Departamento de Atenção Básica. Estratégias para

- o cuidado com a pessoa com doença crônica: diabetes mellitus. Brasília/DF, 2013. [Acesso em 02 de agosto de 2022]. Disponível em:
https://bvsms.saude.gov.br/bvs/publicacoes/estrategias_cuidado_pessoa_diabetes_mellitus_cab36.pdf
6. World Health Organization. Adherence to long-term therapies. Evidence for action. Geneva: WHO; 2003. [Acesso em 01 de Agosto de 2022]. Disponível em:
<https://apps.who.int/iris/bitstream/handle/10665/42682/9241545992.pdf?sequence=1>
 7. Santos AL, Cecílio HPM, Teston EF, Arruda GO, Peternella FMN, Marcon SS. Complicações microvasculares em diabéticos tipo 2 e fatores associados: inquérito telefônico de morbidade autorreferida. *Ciênci saúde coletiva*. 2015;20(3):761-70.
<https://doi.org/10.1590/1413-81232015203.12182014>
 8. de Araújo MF, de Freitas RW, Marinho NB, Alencar AM, Damasceno MM, Zanetti ML. Validation of two methods to evaluate adherence to oral anti-diabetic medication. *J Nurs Healthcare ChronicIllness*. 2011;3:275-82.
<https://doi.org/10.1111/j.1752-9824.2011.01099.x>
 9. Rossi VEC, Silva AL, Fonseca GSS. Adesão ao tratamento medicamentoso entre pessoas com diabetes mellitus tipo 2. *R Enferm Cent O Min*. 2015; 5(3):1820-30. <https://doi.org/10.19175/recom.v5i3.890>
 10. Arrelias CCA, Faria HTG, Teixeira CRS, Santos MA, Zanetti ML. Adesão ao tratamento do diabetes mellitus e variáveis sociodemográficas, clínicas e de controle metabólico. *Acta Paul Enferm*. 2015;28(4):315-22.
<https://doi.org/10.1590/1982-0194201500054>
 11. Carvalho CV, Rocha LP, Carvalho DP, Silva BT, Oliveira SM, Silveira RB. Adesão de pessoas com diabetes mellitus tipo II ao tratamento medicamentoso. *Revenferm UFPE online*. 2017;11(9):3042-9.
<https://doi.org/10.5205/reuol.11088-99027-5-ED.1109201711>
 12. Silva MCM, Barnabe AS, Fornari JV, Ferraz RRN. Avaliação do conhecimento dos portadores de diabetes mellitus sobre a importância da manutenção dos níveis glicêmicos para a prevenção da nefropatia diabética. *SaBios: Rev Saúde e Biol*. 2013;8(3):49-55.
 13. Flor LS, Campos MR. Prevalência de diabetes mellitus e fatores associados na população adulta brasileira: evidências de um inquérito de base populacional. *Rev. bras. epidemiol*. 2017;20(1):16-29.
<https://doi.org/10.1590/1980-5497201700010002>
 14. Machado APMC, Santos ACG, Carvalho KKA, Gondim MPL, Bastos NP, Rocha JVS, et al. Avaliação da adesão ao tratamento de pacientes com diabetes mellitus e seus fatores associados. *Rev Eletrônica Acervo Saúde*. 2019;19:1-10. <https://doi.org/10.25248/reas.e565.2019>
 15. Vicente NG, Goulart BF, Iwamoto HH, Rodrigues LR. Prevalência de adesão ao tratamento medicamentoso de pessoas com diabetes mellitus. *Enferm Global*. 2018;52:460-73. <http://dx.doi.org/10.6018/eglobal.17.4.302481>

16. Malta DC, Duncan BB, Schmidt MI, Machado IE, Silva AG, Bernal RTI, et al. Prevalência de diabetes mellitus determinada pela hemoglobina glicada na população adulta brasileira, Pesquisa Nacional de Saúde. *Rev. bras. epidemiol.* 2019;22(Suppl 2):1-13.
<https://doi.org/10.1590/1980-549720190006.supl.2>
17. Francisco PMSB, Rodrigues PS, Costa KS, Tavares NUL, Tierling VL, Barros MBA, et al. Prevalência de diabetes em adultos e idosos, uso de medicamentos e fontes de obtenção: uma análise comparativa de 2012 e 2016. *Rev. bras. epidemiol.* 2019;22(e190061):1-4. <https://doi.org/10.1590/1980-549720190061>
18. GBD 2016 Brazil Collaborators. Burden of disease in Brazil, 1990-2016: a systematic subnational analysis for the Global Burden of Disease Study 2016. *Lancet.* 2018;392(10149):760-75.
[https://doi.org/10.1016/S0140-6736\(18\)31221-2](https://doi.org/10.1016/S0140-6736(18)31221-2).
19. Bertoldi AD, Kanavos P, França GV, Carraro A, Tejada CA, Hallal PC, et al. Epidemiology, management, complication and costs associated with type 2 diabetes in Brazil: a comprehensive literature review. *Global. Health.* 2013;9(62):1-12. <https://doi.org/10.1186/1744-8603-9-62>.
20. Malta DC, Iser BPM, Andrade SSCA, Moura L, Oliveira TP, Bernal RTI. Tendências da prevalência do diabetes melito autorreferido em adultos nas capitais brasileiras, 2006 a 2012. *Epidemiol Serv Saúde.* 2014;23(4):753-60. <https://doi.org/10.5123/S1679-49742014000400017>
21. Silva AB, Engroff P, Sgnaolin V, Ely LS, Gomes I. Prevalência de diabetes mellitus e adesão medicamentosa em idosos da Estratégia de Saúde da Família de Porto Alegre/RS. *Cad. Saúde Colet.* 2016;24(3):308-16 <https://doi.org/10.1590/1414-462X201600030017>
22. Gomes GJ, Sartori AM, Pereira LMV, Ueta JM, de Oliveira REM. Tratamento e controle de diabetes mellitus tipo 2 em Unidades de Saúde da Família de um município paulista. *Saúde em Redes.* 2021;7(1):1-11.
<https://doi.org/10.18310/2446-4813.2021v7n1p217-227>
23. Maruthur NM, Tseng E, Hutfless S, Wilson LM, Suarez-Cuervo C, Berger Z, Chu Y, et al. Diabetes Medications as Monotherapy or Metformin-Based Combination Therapy for Type 2 Diabetes: A Systematic Review and Meta-analysis. *Ann Internal Med.* 2016;164(11):740-51. <https://doi.org/10.7326/M15-2650>.
24. Nathan DM, Buse JB, Davidson MB, Ferrannini E, Holman RR, Sherwin R, et al. Medical management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement of the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care.* 2009;32:193-203. <https://doi.org/10.2337/dc08-9025>.
25. Faria HTG, Rodrigues FFL, Zanetti ML, Araújo MFM, Damasceno MMC. Factors associated with adherence to treatment of patients with diabetes mellitus. *Acta Paul Enferm.* 2013;26(3):231-7.
<https://doi.org/10.1590/S0103-21002013000300005>
26. King P, Peacock I, Donnelly R. The UK Prospective Diabetes Study (UKPDS): clinical and therapeutic implications

- for type 2 diabetes. *Br J Clin Pharmacol.* 1999;48(5):643-8.
<https://doi.org/10.1046/j.1365-2125.1999.00092.x>
27. Sayin N, Kara N, Pekel G. Ocular complications of diabetes mellitus. *World J Diabetes.* 2015;6:92-108.
<https://doi.org/10.4239/wjd.v6.i1.92>
28. Murussi M, Murussi N, Campagnolo N, Silveiro S. Early detection of diabetic nephropathy. *Arq Bras Endocrinol Metabol.* 2008;52(3):442-51. <https://doi.org/10.1177/14791641211058856>.
29. Boas LCGV, Foss-Freitas MC, Pace AE. Adesão de pessoas com diabetes mellitus tipo 2 ao tratamento medicamentoso. *Ver Bras Enferm.* 2014;67(2):268-73. <https://doi.org/10.5935/0034-7167.20140036>
30. Fischer EB, Thorpe CT, Devellis BM, Devellis RF. Healthy coping, negative emotions, and diabetes management: a systematic review and appraisal. *Diabetes Educator* 2007;33(6):1080-103.
<https://doi.org/10.1177/0145721707309808>.
31. Babenko AY, Mosikian AA, Lebedev DL, Khrabrova EA, Shlyakhto EV. Mental state, psycho emotional status, quality of life and treatment compliance in patients with Type 2 diabetes mellitus. *J Comp Eff Res.* 2019;8(2):113-20. <https://doi.org/10.2217/ce-2018-0105>
32. Capoccia K, Odegard PS, Letassy N. Medication Adherence With Diabetes Medication: A Systematic Review of the Literature. *Diabetes Educ.* 2016;42(1):34-71. <https://doi.org/10.1177/0145721715619038>
33. Thurston MM, Bourg CA, Phillips BB, Huston SA. Impact of health literacy level on aspects of medication non adherence reported by underserved patients with type 2 diabetes. *Diabetes Technol Ther.* 2015;17(3):187-93.
<https://doi.org/10.1089/dia.2014.0220>
34. Bubalo J, Clark RK Jr, Jiing SS, Johnson NB, Miller KA, Clemens Shipman CJ, et al. Medication adherence: Pharmacist perspective. *J Am Pharm Assoc.* 2010;50(3):394-406. <https://doi.org/10.1331/JAPhA.2010.08180>
35. Shoenthaler AM, Schwartz BS, Wood C, Stewart WF. Patient and physician factors associated with adherence to diabetes medications. *Diabetes Educ.* 2012;38(3):397-408. <https://doi.org/10.1177/0145721712440333>
36. Tavares NUL, Bertoldi AD, Mengue SS, Arrais PSD, Luiza VL, Oliveira MA, et al. Fatores associados à baixa adesão ao tratamento farmacológico de doenças crônicas no Brasil. *Rev Saude Publica.* 2016;50(supl 2):1s-10s. <https://doi.org/10.1590/S1518-8787.2016050006150>
37. Constantino MI. Long-term complications and mortality in Young-onset diabetes: type 2 diabetes is more hazardous and lethal than type 1 diabetes. *Diabetes Care* 2013; 36(12):3863-3869.
<https://doi.org/10.2337/dc12-2455>
38. Egede LE, Gebregziabher M, Dismuke CE, Lynch CP, Axon RN, Zhao Y, et al. Medication non adherence in diabetes: longitudinal effects on costs and potential cost savings from improvement. *Diabetes Care.* 2012;

35(12):2533-2530. <https://doi.org/10.2337/dc12-0572>

39. Egede LE, Gebregziabher M, Echols C, Lynch CP. Longitudinal effects of medication non adherence on glycemic control. *Ann Pharmacother*. 2014;48(5):562-570. <https://doi.org/10.1177/1060028014526362>.
40. Wong MC, Wu CH, Wang HH, Li HW, Hui EM, Lam AT, et al. Association between the 8-item Morisky medication adherence scale (MMAS-8) score and glycaemic control among Chinese diabetes patients. *J Clin Pharmacol*. 2015;55(3):279-287. <https://doi.org/10.1002/jcph.408>.
41. Polonsky WH, Henry RR. Poor medication adherence in type 2 diabetes: recognizing the scope of the problem and its key contributors. *Patient Prefer Adherence*. 2016; 22(10):1299-1307. <https://doi.org/10.2147/PPA.S106821>

Contributors

Mendonça IR, Rosendo AB, Silva BB and Iser BPM participated in all stages, from the study conception to the review of the final version of the article.

Conflict of Interest: The authors declare that there is no conflict of interest.

Received: September 19, 2022

Accepted: August 17, 2023