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Higher risk of uncontrolled disease and very poor glycemic control in younger patients with type 2 diabetes

Juan M. López-Navarro[1], *Iván Pérez-Díaz*[1,2*], *Eduardo J. Valladares-Pérez*[2], *Elizabet Sánchez-Landa*[3], *Josette R. Staufert-Gutiérrez*[3], *Arturo Vega-Beyhart*[1] *and Reynerio Fagundo-Sierra*[1]

[1]Department of Internal Medicine, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City; [2]Tecnológico de Monterrey, Monterrey, N.L; [3]Department of Neurosurgery, Hospital de Especialidades, Centro Médico Nacional Siglo XXI, Mexico City; [4]Central Laboratory, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City. Mexico

ABSTRACT

Objective: This research aims to identify the risk factors associated with poor glycemic control in patients with Type 2 diabetes. **Methods:** A retrospective and transversal study was performed comprising patients with Type 2 diabetes mellitus who were classified into four groups according to glycated hemoglobin (HbA1c) level. Patients were considered to have good glycemic control when HbA1c was ≤ 7%. Clinical records were consulted to obtain clinical and laboratory information. Multivariate logistic regression analysis was performed to identify independent risk factors. **Results:** From the final sample (n = 204), associated risk factors for uncontrolled diabetes were < 60 years old (odds ratio [OR] 4.421; 95% confidence interval [CI], 1.991-9.817), < 7 years of education (OR 2.814; 95% CI: 1.337-5.926), ≥ 3 comorbidities (OR 3.556; 95% CI: 1.496-8.453), and history of hypoglycemia (OR 5.406; 95% CI: 1.477-19.790). Age < 50 years (OR 3.737; 95% CI: 1.403-8.357), body mass index > 25 kg/m^2 (OR 23.830; 95% CI: 3.100-183.166), smoking (OR 4.511; 95% CI: 1.917-10.615), and history of diabetic ketoacidosis (OR 4.744; 95% CI: 1.061-21.210) were associated with HbA1c ≥ 12%. **Conclusion:** Uncontrolled disease is more prevalent in patients with low education, three or more comorbidities, and age < 60 years. Daily lifestyle factors, such as nutritional status and smoking, are associated with very

RESUMEN

Objetivo: Identificar los factores de riesgo asociados con un control glucémico deficiente en pacientes con diabetes *mellitus* de tipo 2 (DM2). **Método:** Estudio retrospectivo y transversal en pacientes con DM2, los cuales fueron clasificados en cuatro grupos según el nivel de hemoglobina glucosilada (HbA1c). Se consideró como buen control glucémico un nivel de HbA1c ≤ 7%. Se consultaron los registros clínicos para obtener la información clínica y de laboratorio. Aplicamos un modelo multivariado de regresión logística para identificar los factores de riesgo independientes. **Resultados:** A partir de la muestra final (n = 204), los factores de riesgo asociados con diabetes no controlada fueron: < 60 años (*odds ratio* [OR]: 4.421; intervalo de confianza [IC] del 95%: 1.991-9.817), < 7 años de educación (OR: 2.814; IC 95%: 1.337-5.926), ≥ 3 comorbilidades (OR: 3.556; IC 95%: 1.496-8.453) y antecedente de hipoglucemia (OR: 5.406; IC 95%: 1.477-19.790). Una edad < 50 años (OR: 3.737; IC 95%: 1.403-8.357), un índice de masa corporal (IMC) > 25 kg/m^2 (OR: 23.830; IC 95%: 3.100-183.166), tabaquismo (OR: 4.511; IC 95%: 1.917-10.615) y antecedente de cetoacidosis diabética (OR: 4.744; IC 95%: 1.061-21.210) se asociaron con HbA1c ≥ 12%. **Conclusión:** Existe una mayor prevalencia de descontrol glucémico en pacientes con < 7 años de educación, presencia de tres o

Dirección para correspondencia:
*Iván Pérez-Díaz
E-mail: ivan.endocrino@gmail.com

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Corresponding author: Iván Pérez-Díaz, endocrino@gmail.com

Key words: Diabetes. Risk factors. Glycemic control. Glycated hemoglobin.

más comorbilidades y edad < 60 años. Factores del estilo de vida como IMC > 25 kg/m^2 y tabaquismo se asocian con un control glucémico muy pobre.

Palabras clave: Diabetes. Factores de riesgo. Control glucémico. Hemoglobina glucosilada.

BACKGROUND

Patients with Type 2 diabetes mellitus (T2DM) have an increased risk of death up to 5.2 times higher than the general population, mainly from renal, cardiac, and infectious causes[1]. Controlled randomized studies have shown that intensive glycemic control (glycated hemoglobin [HbA1c] < 7%) reduces the risk of microvascular complications in all patients with T2DM, and in younger patients with recent diagnoses, macrovascular complications are also reduced in a lesser way[2-4]. Despite the established recommendations, the percentage of patients with uncontrolled diabetes is high, varying in different countries from 37.4 to 74.6%[5-7].

A large variety of factors have been associated with poor glycemic control in patients with T2DM such as demographic characteristics, physical activity, nutrition, disease education, sleep habits, smoking, self-care, and glucose monitoring[8-24]. Furthermore, it has been reported that patients with three or more associated comorbidities, frequently attended in reference hospitals, have up to 1.87 times more risk for poor glycemic control[9]. Nevertheless, most of these risk factors have no consistency among studies, suggesting differences in the populations observed. The aim of this study is to identify the risk factors associated with poor glycemic control in Mexican patients with T2DM from a tertiary care hospital.

METHODS

We conducted an observational, transversal, and retrospective study in a tertiary referral hospital approved by the research ethics committee of the institute.

Patients

We included all patients in the hospital's digital database > 18 years with a T2DM diagnosis who had at least one HbA1c measurement (using high-performance liquid chromatography with the programmable electronic system BioRad VARIANT II TURBO HbA1c Kit-2.0 according to National Glycohemoglobin Standardization Program and International Federation of Clinical Chemistry recommendations) and an appointment with a medical caregiver no later than 3 months after their laboratory tests in a study period of 1 year. Our exclusion criterion was an incomplete clinical file. We stratified patients in four groups denominating patients with HbA1c ≥ 12% as those with "very poor control" (VPC), HbA1c 9.1-11.9% "PC", HbA1c 7.1-9% "slight uncontrol" (SC), and HbA1c ≤ 7% "good control" (GC). For the analysis, we included 100% of VPC patients and adjusted the number of patients in each of the other groups to match by simple random sampling.

Variables and definitions

Demographic characteristics, socioeconomic level (SEL), anthropometric measures, laboratory parameters, evolution time (difference between diagnostic and study year), treatment, T2DM complications, and associated comorbidities were taken from the closest clinical record file to the HbA1c measurement of each patient. The SEL was established by Institute's social work department in an ascending scale of 1-7 according to a socioeconomic study,

Table 1. Baseline characteristics in different HbA1C groups

	Good control (HbA1C ≤ 7%)	Slight uncontrol (HbA1C 7.1 ≤ 9%)	Poor control (HbA1C 9.1 < 11.9%)	Very poor control (HbA1C ≥ 12%)	Significant p value
HbA1C %, med (IR)	6.1 (5.6-6.7)	7.9 (7.4-8.3)	10.5 (9.6-11.1)	12.9 (12.4-14)	0.0001[a,d]
Female, n (%)	33 (64.7)	26 (50.98)	31 (60.7)	32 (62.7)	
Age (years), m (± SD)	67.19 (11.13)	63.76 (11.7)	57.25 (9.55)	56.92 (11.26)	0.001[a,d] 0.008[c,e]
< 60 years, n (%)	12 (23.52)	23 (45.09)	33 (64.70)	29 (56.86)	0.000[b,f]
< 50 years, n (%)	4 (7.8)	5 (9.8)	8 (15.7)	12 (23.5)	0.028[c,f]
SEL, med (IR)	3 (2-3)	3 (2-3)	3 (3-3)	3 (2-3)	
Education[g], med (IR)	3 (1-4)	1 (1-3)	2 (1-3)	2 (1-3)	
< 7 years, n (%)	22 (43.13)	31 (60.78)	35 (68.62)	34 (66.66)	0.005[b,f]
BMI[h], m (± SD)	28.72 (7.67)	28.40 (5.79)	28.23 (5.58)	29.27 (6.53)	
SBP, mmHg, med (IR)	125 (105-130)	130 (120-140)	120 (110-140)	120 (110-130)	
DBP, mmHg, med (IR)	70 (65-80)	80 (70-80)	72 (70-80)	76 (67.5-80)	

HbA1C: glycated hemoglobin; med: median; m: mean; SD: standard deviation; IR: interquartile range; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; SEL: socioeconomic level.
[a]Comparison between all the groups. [b]Comparison between good control versus uncontrolled diabetes (HbA1C > 7%). [c]Comparison between very poor control (HbA1C ≥ 12%) versus rest of the patients. [d]Kruskal–Wallis test. [e]Mann–Whitney U test. [f]Pearson's Chi-squared test. [g]Education definitions: 1 = uneducated, 2 = 1-6 years of school, 3 = 7-9 years of school, 4 = 10-12 years of school, 5 = college degree, 6 = postgraduate. [h]Obtained by division of kilograms/height(m)^2.

which represents the percentage of total cost of the service that the patient pays from 4% for level 1 to 115% for level 7. We determined diabetic nephropathy by the presence of albuminuria (urinary albumin-to-creatinine ratio ≥ 30 mg/g) and/or reduced estimated glomerular filtrate rate in the absence of signs or symptoms of other primary causes of kidney damage. Diabetic neuropathy was defined as the loss of protective sensation evaluated by care provider and documented in the clinical record file. The diagnosis of diabetic retinopathy (proliferative or not) was performed by an ophthalmologist[3].

Data analysis

STATA 14.0 (StataCorp LP, Texas, USA) and IBM SPSS Statistics 23 (IBM, New York, USA) software were used to perform statistical analysis. Normal distribution was assessed with obliquity and kurtosis test. Mean (m) and standard deviation were calculated in variables with normal distribution and median (med) and interquartile range (IR) in those with non-normal distribution. The Kruskal–Wallis test was applied to compare independent variables between more than two groups, Pearson's Chi-squared test for independent qualitative variables and the Mann–Whitney U test for quantitative variables between two groups. Spearman's rho correlation was used to compare quantitative variables. Odds ratios (ORs), with 95% confidence interval (CI), were calculated in variables statistically different among groups. Furthermore, multivariate logistic regression analysis was performed with the proposed factors by bivariate analysis. In all cases, $p < 0.05$ was considered statistically significant.

RESULTS

From the database search, we found 899 patients with T2DM diagnosis and an HbA1c measurement

Table 2. Laboratory parameters

	Good control (HBA1C ≤ 7%)	Slight uncontrol (HbA1C 7.1 ≤ 9%)	Poor control (HbA1C 9.1 < 11.9%)	Very poor control (HbA1C ≥ 12%)	Significant p value[a]
Triglycerides mg/dL, med (IR)	129 (92.5-161)	145 (110-198)	162 (117-204)	171 (127-228)	0.0009[b] rho = 0.28[c]
Total cholesterol mg/dL, med (IR)	149.5 (126.7-177-5)	164 (143-196)	178 (152-205)	180 (150-222)	0.0004[b] rho = 0.28[c]
C-HDL mg/dL, med (IR)	41.5 (34.25-54)	43 (36-48)	41 (36-52)	46 (37-57)	
C-LDL mg/dL, med (IR)	88 (58.5-107.2)	90 (74-114)	80 (103-131)	98 (75-135)	0.047[b] rho = 0.17[c]
Glucose mg/dL, med (IR)	108 (92-130)	138 (104-165)	184 (138-245)	294 (215-374)	0.0001[b] rho = 0.62[c]
BUN mg/dL, med (IR)	18.1 (12-24.9)	24.5 (17.7-3)	16.2 (12.9-21.9)	17 (13-27.6)	0.0036[b] rho = 0.076[c]
Creatinine mg/dL, med (IR)	0.86 (0.65-1.23)	1.11 (0.85-1.5)	0.85 (0.65-0.98)	0.79 (0.65-1.13)	0.0026[b] rho = –0.11[c]

HbA1C: glycated hemoglobin; med: median; C: cholesterol; HDL: high-density lipoprotein; LDL: low-density lipoprotein; BUN: blood urea nitrogen; IR: interquartile range. [a]Comparison between all the groups. [b]Kruskal–Wallis test. [c]Spearman correlation.

(n = 899). After grouping patients by glycemic control, 413 patients (46%) had controlled diabetes (HbA1c < 7%) and were enrolled in the GC group; the rest of the patients had uncontrolled disease, of which 281 patients (31.3%) met the grouping criteria for SC group, 154 (17.1%) the PC group and 51 (5.7%) the VPC group. After random sampling, all four groups were confirmed by 51 patients based on the VPC group, analyzing a total of 204 patients (n = 204).

Sociodemographic variables and somatometry

From the final sample, 59.8% (n = 122) of patients were female and the median age of the entire study population was 60 years (IR 53-69.75 years). Patient characteristics by group are found in table 1. There was no difference in gender, SEL, body mass index (BMI), or systolic and diastolic blood pressure among groups. Age had a negative correlation (rho = –0.34, p = 0.000) with patients' HbA1c, finding an OR of 4.063 (95% CI: 1.975-8.357) for having HbA1c > 7% in patients under 60 years old and in patients under 50 years old an OR of 2.462 (95% CI: 1.084-5.590) for presenting HbA1c ≥ 12%.

We observed a trend of lower education levels and poorer glycemic control, but no linear significance was found (p = 0.056). Nevertheless, patients with elementary education (< 7 years of school) had an OR of 2.487 (95% CI: 1.303-4.748) for uncontrolled disease.

Laboratory parameters

A summary of laboratory parameters is found in table 2. Triglycerides (rho = 0.28, p = 0.0001), total cholesterol (rho = 0.28, p = 0.000), low-density lipoprotein (LDL) cholesterol (rho = 0.17, p = 0.0127), and glucose levels (rho = 0.62, p = 0.000) were higher in patients

Table 3. Diabetes evolution time and treatment

	Good control (HbA1C ≤ 7%)	Slight uncontrol (HbA1C 7.1 ≤ 9%)	Poor control (HbA1C 9.1 < 11.9%)	Very poor control (HbA1C ≥ 12%)	Significant p value
Evolution time years, med (IR)	13 (9-23)	17 (9-23)	14 (6-22)	11 (4.5-19)	0.026[b,c]
< 10 years, n (%)	15 (29.4)	13 (25.5)	18 (35.3)	23 (45.1)	0.049[b,d]
Insulin, n (%)	12 (23.53)	32 (62.75)	35 (68.63)	34 (66.67)	0.0001[a,d]
Units/day, med (IR)	18 (0-35)	31.5 (25-37)	34 (20-52)	40 (28-60)	0.004[a,e] rho = 0.28[f]
Metformin, n (%)	35 (68.63)	35 (68.63)	39 (76.47)	35 (68.63)	0.0001[a,d]
mg/day, med (IR)	1,500 (850-2,337.5)	2,550 (1,700-2,550)	2,550 (1,500-2,550)	1,700 (850-2,550)	0.0001[a,e] rho = 0.029[f]

HBA1C: glycated hemoglobin, med: median, IR: interquartile range.
[a]Comparison between all the groups. [b]Comparison between very poor control (HBA1C ≥ 12%) versus rest of the patients. [c]Mann–Whitney U test. [d]Pearson's Chi-squared test. [e]Kruskal–Wallis test. [f]Spearman correlation.

with poorer glycemic control. Blood urea nitrogen and creatinine levels were higher in SC patients than the rest of the groups (p = 0.0036 and p = 0.0026, respectively).

Characteristic disease and treatment

Disease and treatment variables are summarized in table 3. VPC patients had shorter duration of disease (years) since diabetes diagnosis (median 11 years, IR 4.5-19 years; p = 0.026) then the rest of the patients; however, having < 10 years of disease evolution does not increase the risk of an HbA1c ≥ 12% (OR 1.911; 95% CI: 0.997-3.663). More patients with HbA1c > 7% are treated with insulin (67.2%) than patients with GC (23.53%, p = 0.0001). We also observed that higher doses of insulin were needed with poorer glycemic control (median of 18 units for patients in GC, 31.5 in SC, 34 in PC, and 40 in VPC; rho = 0.28; p = 0.001). Patients in the PC group received metformin more frequently (76.47%, p = 0.0001) then all other groups.

Comorbidities

From all groups, 135 patients were overweight or obese (66.1%), finding the highest prevalence (n = 50, 97.62%) in the VPC group (OR 25.298; 95% CI: 3.388-188.907). Linear association was found between smoking prevalence and poorer glycemic control (p = 0.000). Smoking increases the risk for HbA1c > 7% by 3.257 times (95% CI: 1.209-8.772) and 4.288 times for HbA1c ≥ 12% (95% CI: 2.109-8.719). Cirrhosis diagnosis was most prevalent in the VPC group (27.45% vs. 13%; OR 2.516; 95% CI: 1.160-5.457). Renal disease was higher in patients with uncontrolled diabetes (OR 4.231; 95% CI: 1.237-14.473) versus those with good glycemic control. Diagnosis of hypothyroidism was higher in the SC group than the other groups (33.33%, p = 0.023), but no differences were found when comparing patients with good glycemic control versus the uncontrolled group (p = 0.299). The prevalence of hypertension, dyslipidemia, cardiovascular events, cancer, depression, and acute infections was not different among all four groups.

Table 4. Comorbidities and complications of disease.

	Good control (HbA1C ≤ 7%)	Slight uncontrol (HbA1C 7.1 ≤ 9%)	Poor control (HbA1C 9.1 < 11.9%)	Very poor control (HbA1C ≥ 12%)	Significant p value
Comorbidities					
BMI > 25 kg/m^2, n (%)	31 (60.78)	32 (62.74)	31 (60.78)	41 (97.62)	0.000[a,d] 0.000[c,d]
Dyslipidemia, n (%)	33 (64.71)	45 (88.24)	42 (82.35)	33 (64.71)	
Hypertension, n (%)	38 (74.51)	44 (86.27)	36 (70.59)	32 (62.75)	
MACE, n (%)	10 (19.61)	11 (21.57)	7 (13.73)	5 (9.8)	
Smoking, n (%)	5 (9.8)	4 (7.84)	14 (27.45)	22 (43.14)	0.000[a,d] 0.015[b,d] 0.000[c,d]
Cirrhosis, n (%)	5 (9.8)	6 (11.76)	9 (17.65)	14 (27.45)	0.017[c,d]
CKD, n (%)	3 (5.88)	14 (27.45)	8 (15.69)	10 (19.61)	0.034[a,d]
Cancer, n (%)	12 (23.53)	14 (27.45)	5 (9.8)	9 (17.65)	
Hypothyroidism, n (%)	7 (13.73)	17 (33.33)	9 (17.65)	5 (9.8)	0.013[a,d]
Depression, n (%)	11 (21.57)	9 (17.65)	11 (21.57)	9 (17.65)	
Acute infections, n (%)	12 (23.53)	18 (35.29)	13 (25.49)	13 (25.49)	
No. comorbidities, m (DE)	3.27 (1.47)	4.19 (1.66)	3.62 (1.35)	3.78 (1.33)	0.0368[a,e]
≥ 3, n (%)	34 (16.66)	43 (21.07)	42 (20.58)	42 (20.58)	0.013[b,d]
Complications					
Diabetic nephropathy, n (%)	13 (25.49)	31 (60.78)	17 (33.33)	14 (27.45)	0.001[a,d]
Diabetic retinopathy, n (%)	15 (29.41)	27 (52.94)	23 (45.10)	15 (29.41)	0.020[a,d]
Diabetic neuropathy, n (%)	17 (33.33)	22 (43.14)	27 (52.94)	19 (37.25)	
Diabetic foot, n (%)	4 (7.84)	8 (15.69)	8 (15.69)	7 (13.73)	
Hx of hypoglycemia, n (%)	3 (5.88)	9 (17.65)	16 (31.37)	14 (27.45)	0.007[a,d] 0.003[b,d]
Hx of ketoacidosis, n (%)	2 (3.92)	0 (0)	3 (5.88)	6 (11.76)	0.020[c,d]

HbA1C: glycated hemoglobin; BMI: body mass index; m: mean; CKD: chronic kidney disease; MACE: major cardiovascular event; SD: standard deviation; Hx: history. [a]Comparison between all the groups. [b]Comparison between good control versus uncontrolled diabetes (HbA1C > 7%). [c]Comparison between very poor control (HbA1C ≥ 12%) versus rest of the patients. [d]Pearson's Chi-squared test. [e]Kruskal–Wallis test.

Patients with three or more comorbidities had an OR of 2.442 (95% CI: 1.19-5.02) for presenting uncontrolled diabetes. Previous results are summarized in table 4.

T2DM complications

In all patients, diabetic neuropathy (n = 85, 41.66%), diabetic retinopathy (n = 80, 39.21%), and diabetic

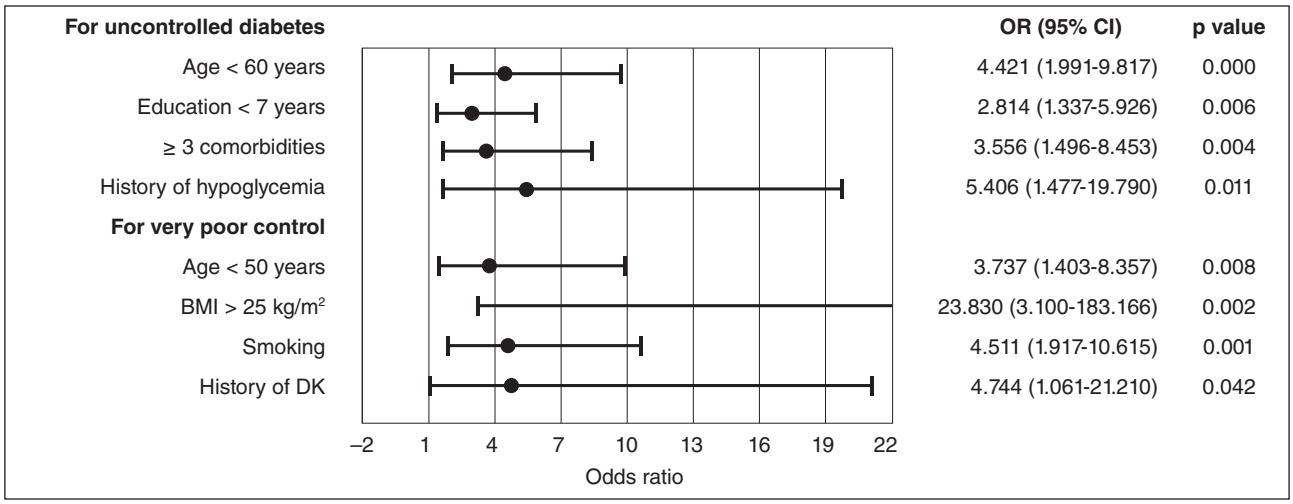

Figure 1. Factors associated with uncontrolled diabetes (HbA1C > 7%) and with very poorly controlled diabetes (HbA1C ≥ 12%). Logistic regression multivariate models. OR: odds ratio; CI: confidence interval; HbA1C: glycated hemoglobin; BMI: body mass index; DK: diabetic ketoacidosis. The uncontrolled diabetes model was adjusted for sex, age, education, nutritional grade, smoking, diagnosis of chronic kidney disease, hypothyroidism, diabetic nephropathy, diabetic retinopathy, history of hypoglycemia, and number of comorbidities. The very poorly controlled model was adjusted for sex, age, education, evolution time, nutritional grade, smoking, diagnosis of hepatic cirrhosis, and history of ketoacidosis.

nephropathy (n = 75, 36.76%) were the most frequent comorbidities. Nephropathy and diabetic retinopathy were more prevalent with poorer glycemic control among all four groups (p = 0.0006, p = 0.02, respectively). Hypoglycemic episodes were more prevalent in uncontrolled patients (HbA1c > 7%) (p = 0.003) having an OR of 5.474 (95% CI: 1.613-18-573) over those with GC. Furthermore, linear association was found between all four groups (5.88% for patients with GC, 17.65% for SC, 31.37% for PC, and 27.45% for VPC; p = 0.002). Patients with HbA1c ≥ 12% had 3.9 times more risk for a ketoacidosis episode than the rest of the groups (95% CI: 1.150-13.541). Peripheral neuropathy and diabetic foot disease were equally prevalent among all groups.

Multivariate analysis

We performed a logistic regression model for uncontrolled diabetes and VPC independently, adjusted for associated factors found in the bivariate analysis. Age < 60 years (OR 4.421; 95% CI: 1.991-9.817), < 7 years of school (OR 2.814; 95% CI: 1.337-5.926), ≥ 3 comorbidities (OR 3.556; 95% CI: 1.496-8.453), and history of hypoglycemia (OR 5.406; 95% CI: 1.477-19.790) resulted in independent risk factors for uncontrolled diabetes. Meanwhile, age < 50 years (OR 3.737; 95% CI: 1.403-8.357), BMI ≥ 25 kg/m^2 (OR 23.830; 95% CI: 3.100-183.166), smoking (OR 4.511; 95% CI: 1.917-10.615), and history of diabetic ketoacidosis (OR 4.744; 95% CI: 1.061-21.210) remain as factors associated with very poor glycemic control (HbA1c ≥ 12%) (Fig. 1).

DISCUSSION

We found a high percentage of patients with uncontrolled diabetes in our population (54%) compared to the described in the United States and Europe (37.4-42.2%)[5-8,11,13]; nonetheless, this number is lower than those reported in Latin American and Asian countries (65.1-74.6%), which could be explained by the specialized diabetes clinics found in our tertiary care institution.

Roy et al. reported that male patients have 2.6 times more risk of having suboptimal glycemic control in T2DM, which was not observed in our analysis. Among Latin American patients, low income has

been associated with worse glycemic control; however, we did not find such association when comparing patients' HbA1c levels and their respective socioeconomic status[10,20].

Age seems to be independently associated with glycemic control; in our population, patients younger than 60 years had 4.4 times more risk for HbA1c > 7%, and those younger than 50 years showed 3.7 times more risk for having HbA1c ≥ 12%. These results support the inverse relation between age and uncontrolled diabetes found in other studies[5,8-13,15,19,20,25], which could be related to poor adherence to treatments, dietetic and physical activity recommendations, or psychological characteristics in younger patients. Although patients with VPC had a shorter evolution time, this finding was not statistically significant in the multivariate analysis. Likewise, a tendency of longer evolution time was observed in the group of patients with uncontrolled disease; therefore, our findings support the progressive beta-pancreatic cell dysfunction as an important factor associated with glucose control[26]. Furthermore, the study design could have influenced the lack of a direct association between HbA1c and the time of evolution, since it is a transversal study where the start time of medical care in the institute and recent hospitalizations was not evaluated. However, a lower age of the patient could be a more important risk factor for presenting VPC than a longer duration of disease because the effect of the latter factor is likely to manifest in lower degrees of uncontrolled diabetes.

In our analysis, we observed that those patients with < 7 years of education have 2.8 times more risk of having an HbA1c > 7%, which could be explained by low disease comprehension and lack of self-care skills[11,14,15,27]. This relation does not persist when comparing patients who left school before the age of 18 and those who continued their studies[5].

In concordance with other studies[10,11], we found worse total cholesterol, LDL cholesterol, and triglyceride levels among patients with poorer glycemic control. Low high-density lipoprotein cholesterol levels have been proposed as an independent risk factor for glycemic uncontrol[28]; nevertheless, we did not find such relation, coinciding with Roy, et al.[10].

We observed that patients with poorer glycemic control received greater insulin doses, which supports other authors' studies[11,29] and suggest the need for a therapeutic response that could impact other related variables like lifestyle intervention, which has been demonstrated to reduce weight in patients with T2DM, having a positive impact on glycemic control[30]. Even without observing differences in BMI among groups in our population, overweight and obese patients show 23 times more risk of VPC, but the 95% CI was very broad, thus a greater sample is needed to make a precise association. Our results are comparable to those of other studies in which BMI has been correlated with poorer glycemic control[25,29], although some others have not found any association[27].

Interestingly, we observed that 41% of patients with cirrhosis had VPC, representing one of every four patients of this group, which demonstrates the lack of glycemic control this population can have. This finding can be explained by the fact that metabolic alterations described in liver disease patients such as elevated fasting leptin, higher insulin resistance, increased gluconeogenesis, diminished hepatic glycogenolysis and a higher glucose sensibility by the pancreatic beta-cells, and increase the difficulty to stabilize their glucose metabolism. Therefore, this group of patients, already susceptible to complications, requires greater vigilance to avoid the catabolic effects of glucose levels close to 300 mg/dL[31].

In the present study, we observed that smoking independently increases by 4.5 times the risk of having HbA1c ≥ 12%. The impact of smoking on glycemic control has been previously reported in a Swedish study, where T2DM smokers have 20% more risk of presenting HbA1c ≥ 6.5%[23]; nevertheless, this observation was not consistent in following studies where the smoking status did not play any role in glycemic control[10,25].

We also found that those patients with ≥ 3 concomitant diseases have 3.5 times more risk of presenting uncontrolled diabetes, which represents a greater risk than the one reported by Lima, et al. (OR 1.87)[9]. A possible explanation points to more medical care

and higher health expenses needed by this specific patient group, which could diminish adherence to the treatment. Regarding comorbidities, a similar study found an association between suboptimal control of T2DM and congestive heart disease and peripheral arterial disease[10].

A higher prevalence of nephropathy and retinopathy resulted in patients with SC, finding a similar frequency of these complications in the GC and VPC groups. This could be because the SC group had the most years of disease evolution, which is a major risk factor for both complications[32,33]. Finally, we observed that patients with uncontrolled diabetes have 5.4 times more risk of having an episode of hypoglycemia, which is associated with higher and more frequent insulin doses[34]. Furthermore, we found that patients with VPC have 4.7 times more risk of having diabetic ketoacidosis, so they should be considered high-risk patients for developing this complication, which highlights the importance of better glycemic control to decrease the incidence in this group.

The nature of the retrospective and transversal study could be a limitation by not including some factors that influence glycemic control such as lifestyle, nutrition, physical activity, treatment adherence, self-care, and psychological aspects. The strength of the present research remains in the methods used to analyze associated factors at different grades of glycemic uncontrol and the fact that patients with HbA1c ≥ 12% were included and analyzed, something that has not been done previously.

Even though there have been advances in the management of T2DM, the prevalence of uncontrolled diabetes in developing countries remains high. In conclusion, uncontrolled disease is more prevalent in patients with low education, three or more comorbidities, and age < 60 years, which emphasizes the need for a multidisciplinary approach offered by medical care institutions. Furthermore, very poor glycemic control is related to factors such as age < 50 years, BMI > 25 kg/m^2, and smoking, highlighting the importance of changes in daily lifestyle. Finally, uncontrolled diabetes and very poor glycemic control are associated with more acute complications such as episodes of hypoglycemia and diabetic ketoacidosis, respectively. Additional studies are needed that evaluate the impact of modification of proposed factors.

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