Cardiovascular risk factors and vascular complications in adults with early- and late-onset diabetes in Mexico. Ensanut 2018

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Abstract

Objective. To inform the prevalence of cardiovascular risk factors and vascular complications in Mexican adults with early- and late-onset diabetes. **Materials and methods.** Information from adults aged 20 years and over participating in the *Encuesta Nacional de Salud y Nutrición* 2018 was used. To compare variables, chi-square tests and Student's t-test were performed. Multiple logistic regression models of having micro and macrovascular complications were obtained. **Results.** Prevalence of diagnosed hypertension on early and late diabetes onset were 37.8 and 51.5%, dyslipidemia 42.6 and 43.8%, tobacco consumption 13.5 and 10.2% and obesity 46.5 and 43.0%, respectively. The average time since diagnosis was 16.9 years for those with early-onset diabetes and 8.9 years for those with late-onset. Peripheral vascular disease in the group with early-onset diabetes was 13.5% (20.2% in those with 10 years and more of diabetes duration), and 5.3% in late-onset diabetes group (7.2% in those with 10 years and more of diabetes duration). **Conclusion.** Adults with early-onset diabetes presented higher proportion of macrovascular

Resumen

Objetivo. Presentar la prevalencia de factores de riesgo cardiovascular, así como de complicaciones vasculares en adultos mexicanos con diabetes de inicio temprano y tardío. **Material y métodos.** Se utilizó información de los adultos de 20 años o más participantes de la Encuesta Nacional de Salud y Nutrición 2018. Para comparar variables se aplicaron pruebas de ji cuadrada y t de Student. Se obtuvieron modelos de regresión logística múltiple de complicaciones micro y macrovasculares. **Resultados.** La prevalencia de hipertensión diagnosticada en diabetes de inicio temprano y tardío fue del 37.8 y 51.5%, de dislipidemia del 42.6 y 43.8; de consumo de tabaco 13.5 y 10.2%, y de obesidad 46.5 y 43%, respectivamente. El tiempo promedio desde el diagnóstico fue de 16.9 años en aquellos con diabetes de inicio temprano y de 8.9 años en aquellos con inicio tardío. La enfermedad vascular periférica en el grupo con diabetes de inicio temprano fue de 13.5% (20.2% en aquellos con 10 años o más con diabetes) y de 5.3% en el grupo de diabetes de inicio tardío (7.2% en aquellos con 10 años o más con diabetes). **Conclusión.**

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complications, probably due to the longer exposure time to hyperglycemia. Patients with early-onset diabetes require intensive treatment to prevent cardiovascular events. Patients with late-onset diabetes require management of age-related comorbidities as hypertension and dyslipidemia.

Keywords: cardiovascular risk factors; onset diabetes; diabetes complications; Ensanut

Los adultos con diabetes de inicio temprano presentaron mayor proporción de complicaciones macrovasculares, probablemente debido al mayor tiempo de exposición a la hiperglucemia. Los pacientes con diabetes de inicio temprano requieren tratamiento intensivo para prevenir complicaciones cardiovasculares. Los pacientes con diabetes de inicio tardío requieren tratamiento de comorbilidades relacionadas con la edad como hipertensión y dislipidemia.

Palabras clave: factores de riesgo cardiovascular; inicio de la diabetes; complicaciones de la diabetes; Ensanut

Due to population growth, aging, urbanization, and the rise in obesity and physical inactivity, the prevalence of type 2 diabetes has increased globally.[1] In 2021, it was estimated that the global prevalence of diabetes in adults aged 20 to 79 years was 10.5% (536.6 million), and by 2045 it is expected to increase to 12.2% (783.2 million).[2]

Since 2000, in Mexico, diabetes has been among the three main causes of death. From the million deaths in our country in 2020, 14% were due to diabetes.[3] The last five *Encuesta Nacional de Salud y Nutrición* (Ensanut) show a stable prevalence of diabetes, going from 14.4% in 2006 to 15.7% in 2020. However, due the increasing size population, the estimated adult people with diabetes increased from 7.3 million (year 2006) to 12.8 million (year 2020).[4] It is estimated that this amount will rise to 21.2 million adults living with diabetes in Mexico by 2045.[2]

In recent years, the onset of type 2 diabetes has occurred more frequently at a younger age.[5] People who develop early-onset type 2 diabetes (age 40 or younger) often have a worst overall profile: obesity, severe dyslipidemia and chronic hyperglycemia compared with people who develop diabetes over the age of 40 (late-onset). However, their prevalence of arterial hypertension is lower. Adults with early-onset diabetes are more likely to develop cardiovascular complications than those with late-onset diabetes.[6] However, some studies have shown that the duration of the disease is the main risk factor for developing diabetes complications, due to the longer time of exposure to hyperglycemia.[7]

Cardiovascular disease remains the leading cause of morbidity and mortality in individuals with diabetes.[8,9] Estimation of cardiovascular risk factors, as dyslipidemia, hypertension, and obesity, and microvascular and macrovascular complications among people with early- and late-onset diabetes is essential to design effective management and intervention strategies.

In this analysis, we inform the prevalence of cardiovascular risk factors and vascular complications in Mexican adults with early- and late-onset diabetes in Mexican adults 20 years and older with early- and late-onset diabetes using data obtained from the Ensanut 2018.

Materials and methods

We conducted a secondary analysis of the Ensanut 2018, which had a cross-sectional design. The sampling was probabilistic, multistage, stratified, and by clusters. Under the sample selection scheme, expansion factors were constructed using the probability of selection and the observed response. The details of the sampling and selection of the sample, as well as the calculation of the expansion factors, were described in a previous publication.[10]

For data collection in the Ensanut 2018, data was obtained through face-to-face interviews, anthropometric measurements, blood pressure, and results of laboratory analysis of blood samples were used. Previously trained and standardized personnel obtained information from 44 612 households, 43 070 questionnaires from adults, 38 433 physical activity questionnaires; from a randomly selected sub-sample of 17 474 adults anthropometric and blood pressure measurement, and from a second randomly selected sub-sample of 12 676 adults a fasting for at least 8 hours blood sample was taken and distributed into tubes BD Vacutainer RST and were immediately stored on ice until a clot was formed and centrifuged at 1 500 rpm for 15 min. Those blood samples were analyzed in the National Institute of Medical Sciences and Nutrition Salvador Zubirán laboratory to obtain glucose, HbA1c, insulin, total cholesterol, HDL, LDL, and triglycerides levels. Glucose, total cholesterol and HDL-C measurements were performed using Synchron CX Delta (Beckman Coulter) colorimetric enzymatic methods. The LDL-C will be calculated with the Sampson`s formula. For the determination of triglycerides, the enzymatic method of glycerol phosphate oxidase was used. High-performance liquid chromatography (HPLC, Variant II Turbo, Bio-Rad) was used to measure glycated hemoglobin (HbA1c). Insulin

was measured by the chemiluminescence method with the Access 2 immunoassay system.

The subjects who participated in the survey signed an informed consent. The Ensanut 2018 protocol was approved by the ethics, research, and biosafety committees of the *Instituto Nacional de Salud Pública*.

In this work, we analyze the information obtained from 12 636 adult's records that have information on the adult's questionnaire, anthropometry, physical activity, and laboratory results. By applying the corresponding expansion factor from the laboratory results database, this sample expands to 79 million adults.

The definition of diabetes was based on adults with previous diagnosis who answered "yes" to the question: "Has a doctor told you that you have diabetes (or high blood sugar)?". The age at the onset of diabetes was obtained from the question: "How old were you when the doctor told you that you had diabetes (or high blood sugar)?". T2DM was defined as early-onset (EO) (≤40 years of age) and late-onset (LO) (>40 years) using the cut-off point recommended by the Joint British Societies-2 (JBS-2) risk guidelines to facilitate the reduction of CVD risk.[11] Time since diagnosis was also obtained by subtracting the age at diagnosis from the age at the time of the interview.

Hypertension was identified by the presence of any of the following conditions: a) adults with previous diagnosis who answered "yes" to the question: "Has a doctor told you that you have high blood pressure?"; or b) if the systolic blood pressure was greater than or equal to 140 mm Hg and/or the diastolic pressure was greater than or equal to 90 mm Hg. Blood pressure was measured in mmHg with a digital sphygmomanometer Omron HEM-907 XL.

For cases of hypercholesterolemia, any person who recognized that a doctor had diagnosed them with high cholesterol and/or had total blood cholesterol levels ≥200 mg/dL was considered. Renal disease and cardiovascular disease were established by reference to the diagnosis made by a physician previously. The presence of diabetes complications was determined by self-report.

The body mass index (BMI) was calculated by dividing the weight in kg by the height expressed in squared meters. A case of obesity was considered when the BMI was greater than or equal to 30 kg/m^2.[12] Abdominal obesity was classified as if the abdominal circumference measurement was ≥ to 88 cm for women and ≥102 for men,[13] and if the circumference was ≥ to 80 cm for women and ≥90 for men.[14]

A person who reported having smoked more than 100 cigarettes up to the time of the interview and who continued to smoke was considered a current smoker. Current physical inactivity was defined as had been physical activity for less than 150 minutes per week, based on the answer of the International Physical Activity Questionnaire (IPAQ) - Short Form.[15] To measure depressive symptoms, the CESD-7 Scale was used, an abbreviated seven-item version of the CES-D Scale, which assesses the frequency with which adolescents and adults have experienced symptoms of depression in the last week. This scale was validated in the Mexican population with a cut-off point of 9 for symptoms indicating moderate or severe depression for adults under 60, and 5 points for adults 60 and over.[16]

Use of medical services was estimated assessing the following variables: screening of obesity, hypertension, and hypercholesterolemia in the last year; prescription of at least one secondary preventive measure (smoking, foot care, vaccination, albuminuria measurement, eye exam, weight loss, exercise 150 minutes/week) and at least one follow up medical visit in the year before. Prediction of having a fatal cardiovascular event in 10-year risk was obtained using the Globorisk laboratory-based risk score, calculated from the results of six variables: sex, age, current smoking status, systolic blood pressure, diabetes, and total cholesterol levels.[17] Subsequently, this variable was categorized according to the risk result: low risk: <10%, medium risk from 10 to <20%, and high risk ≥20%. This risk was obtained only for adults 40 and older who had not experienced a cardiovascular event, such as a heart attack or stroke.

The data for categorical variables are presented as percentages, and those for continuous variables as means and their 95% confidence intervals are presented. To compare the discrete variables results, chi-square tests of independence were performed. To examine the differences in the continuous variables, tests for mean differences were performed using the Student's t-test. To include the effect of time since diabetes diagnoses, we stratified by that variable. Multiple logistic regression models of having micro and macrovascular complications were obtained. Individual weight factors were used in each of the procedures performed. The statistical analysis was carried out with the SVY commands of the STATA 17.0 statistical package, specifying the survey's sampling design to obtain the correct variances.

Results

The prevalence of EO diabetes was 3.5% (95%CI 3.0,4.0) that represent 2.8 million, and of LO was 6.8% (95%CI 6.2,7.5) that represent 5.4 million. Adults with EO diabetes had an average of 16.9 (95%CI 15.3,18.6) years of being diagnosed with diabetes, while the group with LO diabetes had an average of 8.9 (95%CI 8.2,9.6) years since diagnosis. Adults with EO diabetes presented the

highest percentage with more than 10 years since diagnosis (62.4%), the highest average blood glucose levels (188.4 mg/dL) (95%CI 175,201.9), and the highest mean glycosylated hemoglobin values (8.3%) (95%CI 8.0,8.6). Depressive symptoms (37.2%) (95%CI 32.8,41.9) and arterial hypertension (74.5%) (95%CI 69.7,78.7) were more common in adults with LO diabetes compared to those with EO (25.6%) (95%CI 20.5,31.5) and 65.6% (95%CI 58.3,72.3), respectively. 21.1% (95%CI 15.3,28.4) of men and 17.9% (95%CI 12.4,25.1) of women with LO diabetes had high risk of fatal cardiovascular event in 10 years. Higher proportion of adults with LO of diabetes goes for medical visits than adults with EO. Regarding diabetes treatment, about 85% of those with EO and LO diabetes follows pharmacological treatment, most with oral hypoglycemic agents. Insulin is used by 14%, and insulin

with hypoglycemic agents by 16.7% of adults with EO diabetes. Remarkably, adults with EO diabetes presented almost double (18.2%) (95%CI 13.3,24.3) cases with macrovascular complications, including peripheral vascular disease (diabetic foot and amputations) (13.5%) (95%CI 9.6,18.8) than those with LO diabetes (9.7% [95%CI 7.4,12.6] and 5.3% [95%CI 3.0,7.1], respectively) (table I).

Table II shows the distribution of cardiovascular risk factors and diabetes related variables in the study population by the age of onset of diabetes and stratified by diabetes duration. Adults with EO diabetes with 10 years and more since diabetes diagnosis presented the highest prevalence of kidney failure (15.2%) (95%CI 7.7,27.6), and macrovascular complications (25.1%) (95%CI 18.0,33.8), and the highest triglyceride levels 268.8 mg/dL (95%CI 214.8,322.8). Adults with LO and

Table I

Characteristics of adults diagnosed with early and late-onset diabetes. Ensanut 2018, Mexico

	Age of previous diagnosis of diabetes				
	Early (<= 40)		Late >40		
	(n= 518, N= 2.8')		(n= 1 033, N= 5.4')		p value
	%	95%CI	%	95%CI	
Diabetes (%) total	3.5	[3.0,4.0]	6.8	[6.2,7.5]	
Men	1.4	[1.1,1.7]	2.7	[2.3,3.1]	
Women	2.1	[1.7,2.6]	4.1	[3.6,4.7]	
Mean					
Age (years)	49.7	(48.2,51.3)	63.2	(62.0,64.5)	< 0.0001
Age at diagnosis (years)	32.9	(31.8,33.9)	54.1	(53.1,55.1)	< 0.0001
Diabetes duration (years)	16.9	(15.3,18.6)	8.9	(8.2,9.6)	< 0.0001
Glucose (mg/dL)	188.4	(175.0,201.9)	159.9	(152.7,167.2)	< 0.0001
Hba1c (%)	8.3	(8.0,8.6)	7.7	(7.5,7.9)	< 0.0001
Insulin (µU/mL)	15.9	(13.6,18.1)	13.7	(12.4,14.9)	0.006
More than 10 years from diagnosis	62.4	[55.6,68.7]	33.8	[29.6,38.3]	< 0.0001
Parents with diabetes	72.2	[65.6,78.0]	57.7	[52.9,62.3]	0.000
Parents with hypertension	64.1	[56.4,71.1]	58.3	[52.8,63.5]	0.234
Family history of early vascular disease	10.3	[6.9,15.0]	12.2	[9.1,16.1]	0.470
Depressive symptoms	25.6	[20.5,31.5]	37.2	[32.8,41.9]	0.002
Total hypertension	65.6	[58.3,72.3]	74.5	[69.7,78.7]	0.047
Diagnosed hypertension	37.8	[31.3,44.7]	51.5	[46.7,56.4]	0.001
Undiagnosed hypertension	30	[20.1,42.2]	32.8	[26.4,40.0]	0.703
Diagnosis of dyslipidemia	42.6	[35.8,49.8]	43.8	[39.0,48.7]	0.775
Diagnosis of cardiovascular disease	7.6	[4.3,13.1]	7.9	[5.7,10.9]	0.915
Diagnosis of kidney failure	10.1	[5.3,18.6]	2.1	[1.3,3.2]	< 0.0001
Glycosylated hemoglobin >=7%	66	[59.1,72.2]	53.7	[48.9,58.5]	0.005
Physical inactivity	30.2	[23.5,37.9]	21.1	[17.2,25.7]	0.023

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Cardiovascular risk factors					
Current smoker %	13.5	[9.4,18.9]	10.2	[7.6,13.7]	0.247
BMI (kg/m²)*	30.2	(29.4,30.9)	29.9	(29.3,30.4)	0.34
Obesity BMI >=30	46.5	[39.2,53.9]	43	[38.1,48.1]	0.425
Waist circumference (cm)					
Men*	102.4	(100.0,104.7)	102.3	(100.7,103.9)	0.943
Women*	101.5	(99.5,103.6)	101.5	(99.7,103.2)	0.994
Abdominal obesity >88W >102M %	74.7	[68.9,79.7]	72	[67.6,76.0]	0.430
Abdominal obesity >80W >90M %	92.4	[89.1,94.7]	93.5	[90.7,95.5]	0.532
Systolic BP mm Hg*	132.0	(128.6,135.4)	136.5	(134.1,138.9)	0.001
SBP >=140 mmHg %	32.7	[25.3,41.0]	37.7	[33.0,42.7]	0.311
Diastolic BP mm Hg*	78.0	(76.5,79.5)	76.4	(75.1,77.7)	0.009
DBP >=90 mmHg %	12.2	[8.2,17.9]	13.1	[9.9,17.2]	0.774
Total cholesterol (mg/dL)*	193.5	(187.3,199.6)	193.2	(189.6,196.8)	0.923
TCol>=200mg/d %	43.4	[36.4,50.8]	41.5	[36.6,46.6]	0.648
LDL (mg/dL)*	108.3	(103.0,113.7)	113.7	(109.9,117.5)	0.014
ldl>100 mg/dL %	58.3	[49.4,66.8]	64.1	[58.5,69.4]	0.252
HDL (mg/dL)*					
Men	42.1	(39.3,44.8)	38.6	(37.3,40.0)	0.000
Women	43.3	(41.7,44.9)	44.7	(43.3,46.0)	0.033
Hdl <40M <50W%	64	[57.3,70.2]	67.1	[62.4,71.5]	0.422
Triglycerides (mg/dL)*	253.7	(218.3,289.0)	238.2	(218.8,257.5)	0.151
Trig >=150 mg/dL %	70.6	[63.9,76.5]	69.8	[64.9,74.3]	0.852
Globorisk. 10-year risk of fatal cardiovascular event					
Men					
Low risk (<10%)	87.3	[73.4,94.5]	63.1	[55.5,70.2]	
Moderate risk (10% to <20%)	9.5	[3.3,24.7]	15.7	[10.9,22.2]	
High risk (>=20%)	3.2	[1.1,8.6]	21.1	[15.3,28.4]	0.004
Women					
Low risk (<10%)	84.2	[73.7,91.0]	66	[58.3,73.0]	
Moderate risk (10% to <20%)	11.7	[5.7,22.5]	16.1	[12.1,21.1]	
High risk (>=20%)	4.1	[1.9,8.7]	17.9	[12.4,25.1]	0.003
Use of NCD screening services in the last year	21.6	[16.8,27.3]	19.4	[16.0,23.3]	0.488
Following at least one secondary preventive measure	68.8	[62.1,74.8]	69.9	[65.1,74.2]	0.785
Follow up check-ups at least 1 per month	52.1	[44.9,59.2]	62.6	[57.8,67.2]	0.014
Medical treatment					
Pharmacological	84.1	[78.9,88.1]	87	[83.0,90.1]	0.340
Hypoglycemic	53.4	[46.1,60.5]	72.9	[68.4,77.0]	< 0.0001
Insulin	14	[8.7,21.7]	6	[4.1,8.7]	0.006
Hypoglycemics and insulin	16.7	[11.8,23.3]	8.1	[6.3,10.4]	0.001
Diet	32.2	[26.2,39.0]	38.6	[33.9,43.5]	0.134
Exercise	14.6	[10.6,19.9]	13.7	[10.9,17.0]	0.727

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Antihypertensives	81.8	[70.9,89.2]	88.6	[83.3,92.4]	0.162
Statins	40.0	[30.2,50.8]	36.1	[29.3,43.4]	0.53
Fibrates	37.7	[27.9,48.6]	31.5	[24.7,39.3]	0.330
Statins or fibrates	46.7	[37.1,56.6]	42.6	[35.8,49.7]	0.493
Capillary glucose self-monitoring	14.0	[10.0,19.3]	13.1	[10.4,16.5]	0.742
Metabolic control (according with ADA 2016 HbA1, BP, LDL)					
Good control	13.1	[7.9,21.1]	13.9	[10.3,18.5]	0.844
Prevalence of complications					
Microvascular	4.8	[2.9,7.9]	5.9	[3.8,9.0]	0.553
Nephropathy	2.2	[0.9,5.4]	0.9	[0.3,2.4]	0.187
Retinopathy	4	[2.3,7.0]	5.1	[3.2,8.1]	0.509
Macrovascular	18.2	[13.3,24.3]	9.7	[7.4,12.6]	0.002
Cardiovascular disease	5.9	[3.1,11.1]	5.2	[3.4,7.7]	0.739
Heart ischemic disease	4.8	[2.2,10.0]	4.4	[2.8,6.8]	0.283
Stroke	1.2	[0.4,3.9]	1.1	[0.4,2.6]	0.877
Peripheral vascular disease (diabetic foot and amputations)	13.5	[9.6,18.8]	5.3	[3.9,7.1]	< 0.0001

* 95%CI
Ensanut: *Encuesta Nacional de Salud y Nutrición*
BMI: body mass index; BP: blood pressure; Tcol: total cholesterol; LDL: low density lipoprotein cholesterol; HDL: high density lipoprotein cholesterol;
Trig: triglycerides; NCD: non communicable disease; ADA: American Diabetes Association

Table II

CHARACTERISTICS OF ADULTS DIAGNOSED WITH EARLY AND LATE-ONSET DIABETES, AND STRATIFIED BY DIABETES DURATION. ENSANUT 2018, MEXICO

	Age of previous diagnosis of diabetes								
	Early-onset (<= 40)				Late-onset >40				
	Diabetes duration				Diabetes duration				
	< 10 years		>= 10		< 10 years		>= 10		p-value
	(n= 215, N= 1')		(n= 303, N= 1.7')		(n= 670, N= 3.5')		(n= 363, N= 1.8')		
	%	95%CI	%	95%CI	%	95%CI	%	95%CI	
Sex									
Men	42.5	[33.2,52.4]	37.9	[29.1,47.5]	40.6	[35.0,46.5]	37.8	[30.2,46.1]	
Women	57.5	[47.6,66.8]	62.1	[52.5,70.9]	59.4	[53.5,65.0]	62.2	[53.9,69.8]	0.854
Mean									
Age (years)	38.9	(37.8,40.0)	56.3	(54.6,57.9)	60.3	(58.9,61.6)	68.7	(67.2,70.1)	< 0.0001
Age at diagnosis	34.5	(33.5,35.5)	31.8	(30.2,33.4)	55.7	(54.4,57.0)	51.1	(50.0,52.2)	< 0.0001
Diabetes duration	4.4	(3.8, 5.1)	24.5	(22.7,26.3)	4.5	(4.2, 4.9)	17.6	(16.7, 18.4)	< 0.0001
Glucose (mg/dL)	176.2	(161.9,190.5)	195.8	(176.0,215.5)	165.8	(156.8,174.8)	149.7	(139.4,160.0)	< 0.0001
Hba1c (%)	7.9	(7.4,8.4)	8.6	(8.2,9.0)	7.8	(7.5,8.1)	7.6	(7.3,7.9)	< 0.0001
Insulin (µU/mL)	17.1	(14.4,19.8)	15.1	(11.9,18.2)	14.1	(12.6,15.6)	13.1	(10.7,15.5)	0.016
Parents with diabetes	77.5	[68.4,84.5]	68.8	[59.4,76.9]	56.5	[50.3,62.6]	58.4	[49.8,66.6]	0.003
Parents with hypertension	67.7	[58.4,75.7]	61.7	[50.5,71.7]	58.4	[52.0,64.5]	56.2	[46.8,65.2]	0.410
Family history of early vascular disease	8.8	[4.5,16.5]	11.1	[6.8,17.8]	13.2	[9.0,18.8]	11	[7.3,16.1]	0.700
Depressive symptoms	13.5	[7.7,22.6]	32.9	[25.5,41.2]	31.7	[26.8,37.1]	47.3	[38.8,56.0]	< 0.0001

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Total hypertension	51.4	[40.7,62.1]	74.4	[64.8,82.1]	72.3	[66.2,77.6]	79	[69.6,86.0]	0.002
Diagnosis of hypertension	29.3	[20.8,39.4]	42.9	[34.1,52.2]	49.5	[43.6,55.4]	55.2	[46.5,63.5]	0.002
Diagnosis of dyslipidemia	47.7	[38.1,57.6]	39.6	[30.8,49.1]	42.6	[37.0,48.5]	44.3	[36.2,52.7]	0.664
Diagnosis of cardiovascular disease	6.4	[2.4,15.9]	8.4	[4.2,16.1]	7.5	[4.8,11.5]	8.5	[5.1,13.9]	0.949
Diagnosis of kidney failure	1.8	[0.6,5.7]	15.2	[7.7,27.6]	1.4	[0.7,2.6]	3.7	[2.0,6.6]	< 0.0001
Glycosylated hemoglobin >=7%	52.9	[43.1,62.5]	73.8	[65.1,80.9]	53	[47.2,58.6]	56.7	[47.9,65.2]	0.001
Physical inactivity	20.1	[14.3,27.7]	37.1	[27.2,48.3]	15.4	[11.9,19.7]	34.8	[25.5,45.4]	< 0.0001
5 alcohol drinks at least once per month	12.4	[7.8,19.1]	5.6	[2.7,11.2]	8	[5.7,11.2]	7.3	[3.6,14.4]	0.320
Cardiovascular risk factors									
Current smoker %	14.2	[8.9,22.0]	13.0	[7.8,21.0]	9.8	[6.6,14.3]	11.7	[7.0,18.9]	0.667
BMI (kg/m²)*	32.6	(31.5,33.7)	28.5	(27.7,29.3)	30.2	(29.6,30.9)	29	(27.9,30.2)	< 0.0001
Obesity BMI >=30	69.7	[61.0,77.3]	30.8	[22.9,40.0]	46.4	[40.4,52.5]	34.8	[27.1,43.4]	< 0.0001
Waist circumference (cm)									
Men*	104.9	(101.6,108.3)	100.4	(97.2,103.5)	102.3	(100.5,104.1)	102.5	(99.2,105.7)	0.072
Women*	105.1	(101.8,108.4)	99.3	(96.8,101.6)	101.6	(99.6,103.5)	101.1	(97.8,104.5)	0.003
Abdominal obesity >88W >102M %	77.9	[70.0,84.3]	72.5	[64.2,79.5]	71.9	[66.0,77.2]	72.1	[63.5,79.4]	0.707
Abdominal obesity >80W >90M %	92.6	[86.6,96.0]	92.2	[87.9,95.1]	94.2	[91.1,96.3]	92.6	[85.9,96.3]	0.8
Systolic BP mm Hg*	122.5	(119.0,126.1)	137.9	(133.5,142.3)	135.5	(132.3,138.7)	139.4	(135.7,143.1)	< 0.0001
SBP >=140 mmHg %	11.7	[6.8,19.5]	45.7	[35.5,56.3]	34.3	[28.8,40.3]	46.5	[37.5,55.9]	0
Diastolic BP mm Hg*	79.3	(77.7,81.0)	77.1	(75.0,79.2)	77.7	(76.0,79.4)	73.7	(71.6,75.9)	< 0.0001
DBP >=90 mmHg %	10.0	[6.2,15.6]	13.7	[8.0,22.3]	14.8	[11.0,19.7]	7.9	[3.9,15.4]	0.229
Total cholesterol (mg/dL)*	191.1	(181.4,200.8)	194.9	(187.1,202.7)	194.5	(190.2,198.8)	191	(184.8,197.3)	0.503
Cholt>=200mg/d %	40.8	[31.6,50.7]	45.1	[35.4,55.1]	42.4	[36.8,48.2]	39.1	[30.9,48.1]	0.790
LDL (mg/dL)*	107.6	(97.8,117.4)	108.8	(102.7,115.0)	114.4	(110.4,118.5)	111.8	(104.0,119.5)	0.079
ldl>100 mg/dL %	56.9	[43.7,69.2]	59.3	[47.4,70.2]	67.9	[61.1,73.9]	57.7	[47.7,67.0]	0.229
HDL (mg/dL)*									
Men	43.4	(38.2,48.6)	41.1	(38.4,43.7)	37.5	(36.1,38.9)	41.1	(38.8,43.3)	< 0.0001
Women	42.0	(39.6,44.4)	43.9	(41.9,45.9)	44.8	(43.4,46.3)	44.3	(41.9,46.7)	0.052
Hdl <40M <50W%	61.4	[51.1,70.8]	65.5	[56.7,73.4]	68	[62.4,73.1]	64.4	[56.0,72.1]	0.684
Triglycerides (mg/dL)*	228.8	(203.6,254.1)	268.8	(214.8,322.8)	247.8	(221.4,274.1)	222.5	(197.0,248.0)	0.016
Trig >=150 mg/dL %	68.0	[57.7,76.9]	72.2	[63.6,79.4]	72.3	[66.7,77.3]	66.6	[57.5,74.6]	0.617
Use of NCD screening services in the last year	30.8	[22.4,40.5]	16.1	[11.1,22.9]	21.2	[16.8,26.3]	16.4	[11.5,22.8]	0.022
Following at least one secondary preventive measure	62.5	[52.0,71.9]	72.7	[63.9,80.0]	69.1	[63.6,74.2]	73.2	[65.1,80.1]	0.326
Follow up check-ups at least 1 per month	43.9	[34.3,54.0]	57.1	[47.4,66.3]	59.9	[54.1,65.4]	69.1	[61.2,76.0]	0.003
Medical treatment									
Pharmacological	70.7	[60.8,79.0]	92.1	[87.1,95.3]	84.2	[79.5,87.9]	92.3	[82.3,96.9]	0.001
Hypoglycemic	57.2	[46.8,67.0]	51.0	[41.5,60.4]	75.0	[69.7,79.6]	68.5	[59.8,76.1]	< 0.0001
Insulin	7.6	[3.0,18.0]	17.8	[10.3,29.0]	3.4	[1.8,6.4]	11.1	[6.8,17.5]	0.001
Hypoglycemics and insulin	5.8	[3.1,10.7]	23.3	[15.8,33.0]	5.8	[3.8,8.6]	12.8	[9.1,17.6]	< 0.0001
Diet	29.2	[21.0,38.9]	34.1	[26.0,43.3]	33.0	[27.8,38.7]	48.0	[39.5,56.5]	0.011
Exercise	17.0	[9.9,27.7]	13.2	[8.9,19.1]	14.7	[11.1,19.2]	11.3	[7.8,16.1]	0.968
Antihypertensives	69.7	[54.0,81.8]	86.5	[69.8,94.7]	83.9	[76.2,89.4]	96.2	[90.3,98.6]	0.013
Statins	27.5	[14.8,45.3]	49.5	[36.6,62.6]	37.2	[29.0,46.2]	36.5	[26.0,48.5]	0.198
Fibrates	22.9	[13.6,36.0]	47.9	[33.6,62.4]	31.5	[23.3,41.0]	29.2	[19.4,41.5]	0.050

(continuation)

Statins or fibrates	36.3	[23.4,51.6]	54.1	[40.9,66.8]	42.4	[34.4,50.8]	42.1	[31.5,53.6]	0.277
Capillary glucose self-monitoring	12.2	[7.4,19.5]	15.2	[9.8,22.9]	13.0	[9.5,17.6]	14.1	[9.7,20.0]	0.894
Metabolic control (according with ADA 2016 HbA1, BP, LDL)									
Good control	21.0	[10.6,37.3]	8.1	[4.0,15.6]	15.2	[10.5,21.6]	10.8	[6.5,17.3]	0.139
Prevalence of complications									
Microvascular	2.8	[1.0,7.1]	6.1	[3.4,10.6]	5.0	[2.8,8.8]	7.4	[3.7,14.3]	0.460
Macrovascular	6.8	[2.7,16.3]	25.1	[18.0,33.8]	8.8	[6.1,12.6]	11.9	[8.2,16.9]	< 0.0001
Cardiovascular disease	4.8	[1.4,15.4]	6.6	[3.0,13.7]	5.1	[2.9,8.8]	5.7	[3.3,9.7]	0.936
Peripheral vascular disease (diabetic foot and amputations)	2.4	[0.9,6.6]	20.2	[14.0,28.2]	4.1	[2.7,6.3]	7.6	[4.9,11.7]	< 0.0001

* 95%CI
Ensanut: *Encuesta Nacional de Salud y Nutrición*
BMI: body mass index; BP: blood pressure; Tcol: total cholesterol; LDL: low density lipoprotein cholesterol; HDL: high density lipoprotein cholesterol;
Trig: triglycerides; NCD: non communicable disease; ADA: American Diabetes Association

10 years or more since diabetes diagnosis had the highest prevalence of depressive symptoms (47.3%) (95%CI 38.8,56.0) and hypertension (79%) (95%CI 69.9,86). Although adults with EO diabetes, with less than 10 years since diabetes diagnosis, had the highest obesity prevalence (69.7%) (95%CI 61,77.3), they presented the highest percentage of adults with good glycemic control (21%) (95%CI 10.6,37.3).

In table III we present the odds ratio (OR) of having diabetes complications in adults with EO compared with LO. Diabetes duration was a significant risk of both microvascular and macrovascular complications, OR was significative in almost all models presented. Early onset diabetes was associated with the presence of macrovascular complications, only in model 1, adjusted by sex and age (OR= 3.06, 95%CI 1.68,5.57). Men had 60% more risk of having macrovascular complications than women.

Discussion

In a national representative sample of adults from Mexico, we found higher prevalence of hypertension, abdominal obesity, hypertriglyceridemia, and hypoalphalipoproteinemia in those with diagnostic of diabetes. We also found higher prevalence of macrovascular complications and kidney failure in adults with early-onset of diabetes, and higher prevalence of age-related comorbidities as hypertension, depressive symptoms, and mean LDLC levels in adults with late-onset of diabetes. Another difference between adults with early-onset and late-onset diabetes that in our study population is the length of time they have been exposed to the disease. While those with onset after 40 years of age have an average of 8.9 years with the disease and, those with early-onset diabetes have an average of 16.9 years with the diagnosis, 62.4% of this last group have had the disease for over 10 years. By diabetes duration stratification, adults with early-onset diabetes with 10 years and more since diabetes diagnostic had higher mean glucose, HbA1 and triglycerides levels; higher prevalence of kidney failure and macrovascular complications, mainly due by diabetic foot and amputations; they also had the lowest percentage of metabolic control.

Epidemiological studies have shown that the increased risk of developing complications associated with early-onset diabetes is attributed to the longer hyperglycemic exposure time.[18] Regarding cardiovascular complications, approximately 10% of those who develop type 2 diabetes before the age of 30 may develop severe complications, such as atherosclerotic vascular disease, without presenting previous symptoms.[19] As diabetes screening becomes more widespread, the age of diagnosis for diabetes is likely to decrease. Prolonged type 2 diabetes could lead to reduced β cell function and increased HbA1c concentrations, increasing systolic blood pressure and LDL-C concentrations due to increased oxidative stress and system renin-angiotensin activation, accelerating atherosclerosis, and increasing the risk of CVD.[20] Another possible explanation is that people with younger-onset type 2 diabetes are likely to be obese and have higher blood glucose levels, poorer glycemic control, and lower adherence to therapy compared with those diagnosed later.[21] The prolonged duration of diabetes and the worsening metabolic profile could explain most, but not all, the increased risk of cardiovascular disease.[6]

Table III
Adjusted logistic regression models of having diabetes complications in adults with early-onset versus late-onset. Ensanut 2018, Mexico

Complications	Model 1		Model 2		Model 3		Model 4	
	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Microvascular								
Early vs late onset	1.22	0.45,3.35	0.72	0.20,2.52	0.71	0.21,2.40	0.71	0.20,2.50
Sex (men)	1.37	0.68,2.77	1.26	0.63,2.54	1.25	0.63,2.49	1.28	0.63,2.59
Age (1 year increase)	1.03	0.98,1.08	1.02	0.96,1.08	1.02	0.97,1.07	1.02	0.96,1.07
Diabetes duration (1 year increase)			1.03	1.00,1.07	1.03	1.00,1.07	1.03	0.99,1.07
LDL					0.89	0.46,1.70	0.88	0.45,1.71
Hypertension							1.50	0.47,4.73
Macrovascular								
Early vs late onset	3.06	1.68,5.57	1.78	0.82,3.84	1.79	0.83,3.89	1.94	0.90,4.22
Sex (men)	1.66	1.05,2.62	1.63	1.03,2.59	1.64	1.03,2.60	1.66	1.03,2.67
Age (1 year increase)	1.03	1.01,1.05	1.01	0.99,1.03	1.01	0.99,1.03	1.00	0.98,1.03
Diabetes duration (1 year increase)			1.03	1.00,1.05	1.03	1.00,1.05	1.03	1.00,1.06
LDL					1.08	0.68,1.73	1.12	0.69,1.81
Hypertension							2.88	1.58,5.25

Ensanut: *Encuesta Nacional de Salud y Nutrición*
OR: odds ratio; LDL: low density lipoprotein cholesterol

Other studies have shown that arterial hypertension is one of the most prevalent triggers for cardiovascular disease.[22] Hypertension occurs more frequently in the population with diabetes. These two comorbidities have common risk factors, such as insulin resistance, dyslipidemia, and obesity. When both morbidities are present, vascular damage and endothelial dysfunction increase. These lead to micro and macrovascular diseases, predisposing to the development of cardiovascular disease.[23] The results of this study show that hypertension is a cardiovascular risk factor with a high prevalence in the Mexican population living with diabetes, especially in those with late-onset diabetes. Just over 80% of adults with diagnosed diabetes take some type of antihypertensive medication.

Another highly prevalent risk factor is obesity. Obesity is a factor that favors the development of most chronic diseases, such as diabetes, arterial hypertension, and cardiovascular diseases. In addition, the obesity constitutes a public health problem by itself. In our study population, obesity occurs to a greater extent in subjects with early-onset diabetes with less than ten years since diagnostic.

The prevalence of hypertriglyceridemia, close to 70%, hypoalphalipoproteinemia, close to 65%, and previous diagnosis of dyslipidemia, close to 40%, do not show differences due to the age of onset of diabetes. The use of statins and fibrates to control these diseases is at a low rate.

A significant fact observed in the population aged 20 years and over in our country is the decrease in the prevalence of current smoking, from 22.2% found in the *Encuesta Nacional de Salud* (Ensa) 2000,[24] 19.9% in Ensanut 2012,[25] to 17.9% in the Ensanut 2018,[26] which may be a reflection that the campaigns against this risk factor promoted in the last five years by the health sector have had a positive impact.

Several studies have shown that cardiovascular risk factors are interrelated, which is why it is relatively common to find various factors in the same person. Of the adult population of Mexico, 93.8% has at least one cardiovascular risk factor (current smoker, abdominal obesity, systolic blood pressure ≥140, total cholesterol ≥200, LDL-C ≥100, HDL-C >40 in men and >50 in women, triglycerides ≥150). In other words, just over 48 million Mexican adults had at least one cardiovascular risk factor. But even more worrying is that 29.4% of the population presented four or more cardiovascular risk factors. This data shows the situation in which this population finds itself since there is the possibility that they are in the advanced stages of these comorbidities. These complications imply high direct or indirect costs

for individuals and health institutions, and the risk of dying from cardiovascular disease increases.[27] CVD is a major cause of mortality among people with T2DM, is estimated that cause half of deaths in these patients.[28]

Considering that in our country, cardiovascular diseases have been the main cause of death since 1990, and due to the increase in the prevalence of cardiovascular risk factors (diabetes, obesity, and dyslipidemia) in recent years, it is necessary to implement educational and preventive programs that modify the lifestyles that a large part of the Mexican population currently follows, as well as continuing with the anti-smoking program in the general population. Likewise, it is important to ensure that people with diagnosed pathologies, such as arterial hypertension, diabetes mellitus, and hypercholesterolemia receive adequate treatment and control, to avoid or delay the onset of their complications.

Among the main advantages of this study are the sample size and the survey design. Both allow us to make inferences from a nationally representative sample. The interviewers and those who took measurements and blood samples were trained and standardized to avoid measurement bias. Within the limitations, we have that due to the cross-sectional design of this study, we cannot infer causal associations. Except for anthropometric measurements, blood pressure, and laboratory results, the information on diabetes, physical activity, and diagnosis of other diseases was obtained from the answers given by the interviewee and not from the verification of information from the medical history.

The NOM-015-SSA2-2010,[29] for the prevention, treatment, and control of diabetes mellitus establishes that in each visit to the medical service, patients with diabetes must be evaluated for metabolic control, the eating plan and the physical activity, as well as intentionally investigate the presence of complications. Weight, blood pressure, and the result of the foot examination are recorded. However, we can see a substantial proportion of adults with diagnosed diabetes and hypertension, even without a diagnosis.

The 2019 clinical practice guideline for the Prevention, diagnosis, outpatient control targets, and timely referral of type 2 DM at the first level of care[30] recommends applying a cardiovascular risk assessment tool at the start of DM treatment. DM2, to determine the pharmacological and non-pharmacological management and avoid the development of complications. The Mexican Society of Cardiology[31] recommends the clinical use of the Globorisk mathematical model validated with the Mexican population. In this population, 3.2% of men and 4.1% of women with early-onset diabetes and 21.1% of men and 17.9% of women with late-onset diabetes have a high risk (greater than 20%) of presenting a fatal cardiovascular event in the next 10 years. A limitation in using actual cardiovascular risk score that does not include diabetes duration and assign a great weight to patient age, could underestimate the risk.

Our study shows that cardiovascular risk factors are distributed differentially among Mexican adults over 20 with early-onset diabetes compared to late-onset diabetes. Adults with early-onset diabetes presented a higher proportion of macrovascular complications, probably due to the longer exposure time to hyperglycemia, compared to those with late-onset diabetes. It is important to increase the detection of diabetes, especially at an early age. Despite the increase in the proportion of patients receiving pharmacological treatment, it is necessary to improve glycemic control in these patients, and particularly people diagnosed with type 2 diabetes at a younger age may have been treated more intensively and require intensive lifestyle interventions. Patients with late-onset diabetes require management of age-related comorbidities. The use of a cardiovascular risk score is recommended to guide the pharmacological treatment of comorbidities and avoid the development of complications. It is necessary to continue studying the prevalence of cardiovascular risk factors periodically to design and propose strategies for their prevention and control.

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