Prediabetes, undiagnosed T2D, insulin resistance and metabolic syndrome in Guanajuato, Mexico

Rodolfo Guardado-Mendoza, MD, PhD,[1,*] Katya Vargas-Ortiz, PhD,[2,*] María de Lourdes Reyes-Escodigo, PhD,[1] Rafael Rodríguez-Cortés, MSc,[1] Lola Evia-Viscarra, MSc.[3]

Guardado-Mendoza R, Vargas-Ortiz K, Reyes-Escodigo ML, Rodríguez-Cortés R, Evia-Viscarra L.
Prediabetes, undiagnosed T2D, insulin resistance and metabolic syndrome in Guanajuato, Mexico.
Salud Publica Mex. 2024;66:288-295.
https://doi.org/10.21149/15414

Abstract

Objective. To evaluate the prevalence of prediabetes (PD), undiagnosed type 2 diabetes (T2D), metabolic syndrome (MetS), and insulin resistance (IR) as well as related risk factors in Mexican population from Guanajuato, Mexico. **Materials and methods.** We performed a cross-sectional study in the Mexican population from León, Guanajuato, Mexico. A clinical and metabolic evaluation was performed with an oral glucose test (OGTT); PD, undiagnosed T2D, MetS, and IR were identified according to international guidelines. **Results.** Of the 1 470 participants included, 32.9% had PD, 8.4% undiagnosed T2D, 48.1% MetS, and 55.7% IR. Main risk factors associated with T2D and PD were central obesity, overweight, acanthosis nigricans, family history of T2D and age. **Conclusions.** The prevalence of glucose abnormalities, MetS, and IR are high in the Mexican population, and this is related to the high frequency of multiple risk factors in our population.

Keywords: prediabetes; undiagnosed diabetes; insulin resistance; metabolic syndrome

Guardado-Mendoza R, Vargas-Ortiz K, Reyes-Escodigo ML, Rodríguez-Cortés R, Evia-Viscarra L.
Prediabetes, DT2 no diagnosticada, resistencia a la insulina y síndrome metabólico en Guanajuato, México.
Salud Publica Mex. 2024;66:288-295.
https://doi.org/10.21149/15414

Resumen

Objetivo. Evaluar la prevalencia de prediabetes (PD), diabetes tipo 2 no diagnosticada (DT2), síndrome metabólico, y resistencia a la insulina, así como los factores de riesgo asociados en población mexicana de Guanajuato, México. **Material y métodos.** Estudio transversal en población mexicana de León, Guanajuato, México. Se realizó una evaluación clínica y metabólica mediante curva de tolerancia oral a la glucosa; la definición de PD, DT2, síndrome metabólico y resistencia a la insulina se hizo de acuerdo a lineamientos internacionales. **Resultados.** De los 1 470 participantes incluidos, 32.9% tuvieron PD, 8.4% DT2, 48.1% síndrome metabólico, y 55.7% resistencia a la insulina. Los principales factores de riesgo asociados con DT2 y PD fueron obesidad central, sobrepeso, acantosis nigricans, historia familiar de DT2, y edad. **Conclusiones.** La prevalencia de anormalidades en la glucosa, síndrome metabólico y RI son altas en población mexicana, y esto está relacionado con la alta prevalencia de múltiples factores de riesgo en nuestra población.

Palabras claves: prediabetes; diabetes no diagnosticada; resistencia a la insulina; síndrome metabólico

* Guardado-Mendoza and Vargas-Ortiz contributed equally to this article.

(1) Laboratorio de Investigación del Metabolismo, Departamento de Medicina y Nutrición, Universidad de Guanajuato. León, Guanajuato, Mexico.
(2) Departamento de Ciencias Médicas, Universidad de Guanajuato. León, Guanajuato, Mexico.
(3) Departamento de Endocrinología Pediátrica, Hospital Regional de Alta Especialidad del Bajío. León, Guanajuato, Mexico.

Received on: October 30, 2023 • **Accepted on:** February 16, 2024 • **Published online:** April 29, 2024
Corresponding author: Rodolfo Guardado-Mendoza. Laboratorio de Investigación del Metabolismo, Departamento de Medicina y Nutrición, Universidad de Guanajuato. Blvd. Puente MIlenio 1001, Fracción del Predio San Carlos. 37670 León, Guanajuato, Mexico.
email: rguardado@ugto.mx

Type 2 diabetes (T2D) accounts for 90-95% of all diabetes types and includes people who have a relative insulin deficiency and peripheral insulin resistance (IR). The global prevalence of T2D in Mexico in population > 20 years of age has been estimated to be more than 10%. This prevalence is higher in women (11.4%) than in men (9.1%).[1] According to a population health survey, 25% increase in T2D was detected in a period of 7 years, and it has been estimated that around 50% of people with T2D don't know they have the disease.[2] The International Diabetes Federation (IDF) estimated that North America and the Caribbean region spent USD 414.5 billion on diabetes in 2021 and its prevalence will increase by 24% (from 51 to 63 million) by 2045.[3]

Prediabetes (PD) is a condition that appears before the onset of T2D. According to the American Diabetes Association (ADA) criteria, PD is diagnosed with fasting plasma glucose (FPG) 100 to 125 mg/l (impaired fasting glucose [IFG]) or 2 h glucose levels during oral glucose tolerance test (OGTT) between140 and 199 mg/dl (impaired glucose tolerance [IGT]) or HBA1C 5.7 to 6.4%. Each of these criteria places individuals at increased risk of developing T2D and its complications. The incidence of T2D in subjects with IFG or ITG is 4 to 6% every year, however, in patients with mixed prediabetes (IFG + IGT), the risk of developing T2D increases to 10%.[4] The prevalence of IFG and IGT varies internationally by ethnicity; the IGT global prevalence in adults aged 20 to 79 years has been estimated at 7.3%.[5] In Mexico, a PD prevalence of 15-22% has been reported in young adults.[6]

Different risk factors may be associated with PD and T2D: body mass index (BMI) >25 kg/m^2, first-degree relative with T2D, high-risk race/ethnicity, history of cardiovascular disease (CVD), hypertension, low concentration of HDL cholesterol and/or a high concentration of triglyceride, physical inactivity, acanthosis nigricans, HbA1C ≥5.7%, age ≥45, women with polycystic ovary syndrome and those who were diagnosed with gestational diabetes mellitus (GDM).[7]

However, the global prevalence of T2D and PD varies according to population and diagnostic tool used, fasting glucose and 2h glucose post-OGTT or HbA1C mean something different from a physiopathological standpoint. The goal of this work was to evaluate the prevalence of prediabetes, undiagnosed T2D, metabolic syndrome (MetS), and IR, as well as the associated risk factors in adult Mexican patients from León, Guanajuato, Mexico.

Materials and methods

Subjects

The study population included 1 470 subjects without a known diagnosis of T2D or prediabetes 18-65 years of age from León, Guanajuato, Mexico. Patients were not included if they were taking medications that affect glucose metabolism, if they were pregnant or if they reported any other severe illness that influences glucose metabolism. Patients were included by a non-random sampling from the general population and from workers at the University and their families who were invited to participate in a general metabolic evaluation; patients were invited to participate in the study through informative spots in different Departments from the University of Guanajuato performed by the research team. The average range of acceptance from those invited to participate in the study was between 85-90%. Data were collected between September 2014 and October 2019.

Study design

This was a cross-sectional analysis derived from the Metabolic University Cohort conducted at the *Laboratorio de Investigación del Metabolismo*, *Departamento de Medicina y Nutrición*, University of Guanajuato, Mexico. The study protocol was approved by the Research Council at The University of Guanajuato (THR/DMN-MC/56/12). Written informed consent was signed by all participants. All patients attended the *Laboratorio de Investigación del Metabolismo* at the University of Guanajuato for a metabolic evaluation, and a clinical history and a physical examination were performed to identify T2D risk factors.

Anthropometrical measurements

Weight and height were measured while participants were barefoot and wearing minimal clothing with their shoulders in a normal position. BMI was obtained from standardized measurements of weight and height and was computed as a ratio of weight (kg): height squared (m^2). Waist circumference was measured at the high point of the iliac crest at the end of normal expiration to the nearest 0.1 cm, and it was considered high when it was ≥90cm in men and ≥80cm in women. Body composition (body fat percentage and visceral index) was

assessed with electrical bioimpedance through a Tanita Scale SC-240. All measurements were performed by personnel trained to use standardized procedures and reproducibility was evaluated, resulting in concordance coefficients between 0.88 and 0.94.

Clinical and metabolic evaluation

Resting blood pressure was measured twice using the auscultatory method using a sphygmomanometer in the seated position (HEM-714; Omron Healthcare, Inc., USA). Patients reporting previous diagnosis of HBP, use of antihypertensive medications or SBP ≥140mmHg and/or DBP ≥90mmHg, were considered hypertensive. The average of two blood pressure measures was used in the analysis.

Oral glucose tolerance test (OGTT): All subjects were admitted to the *Laboratorio de Investigación del Metabolismo* on the day of the study between 7 and 8 AM, and after 8-10 h fasting; a catheter was placed into an antecubital vein for all blood withdrawal. Subjects will not be allowed to eat or drink anything after 10 PM on the night before until the study is completed. After the intravenous catheter was placed and the first blood sample was drawn, the patients ingested 75 g of glucose. Plasma samples for glucose measurement were drawn at 0 min and every 30 min thereafter for two hours. Lipid levels were obtained at fasting and together with glucose were measured by a colorimetric method (Kodak Ektachem DT60II).

T2D was diagnosed with FPG ≥126 mg/dl or 2-h plasma glucose (PG) ≥200mg/dl during OGTT. Prediabetes was diagnosed with FPG 100 to 125 mg/l or 2-h PG during OGTT 140 to 199 mg/dl.[7] MetS was defined by having three or more of the following criteria: triglycerides levels ≥150mg/dl, low HDL-cholesterol <40 mg/dl in men and <50 mg/dl in women; high blood pressure ≥130/85mmHg, hyperglycemia ≥100 mg/dl, and waist circumference ≥90 cm in men and ≥80cm in women.[8,9] IR was calculated as reported by Matthews and colleagues,[10] and a value ≥2.0 was used to define IR.[11] Risk factors for hyperglycemia were obtained according to the American Diabetes Association recommendations.[7]

Statistical analysis

Data are reported as means and percentages. Inter-group differences were assessed by one-way ANOVA with the Bonferroni Post Hoc test. Qualitative variables were compared by Pearson's chi-square. Association between variables was assessed by odds ratio and by multiple logistic regression analysis, including as a predictor the main T2D risk factors; interactions between all risk factors for T2D were evaluated. A minimum sample size of 976 subjects was needed to identify a 22.1 ± 2.6% prevalence of prediabetes and a 5.8 ± 1.5% of new T2D with a 95% confidence level, according to recent publications in Mexican population.[12] A p-value < 0.05 was considered statistically significant. SPSS, version 21 was used to perform statistical analysis.

Results

A total of 1 598 patients were screened to participate in the study, but only 1 470 meet the eligibility criteria. The average age was 41 ± 13 years; there were 64.8% females and 35.2% males. From the total studied population, 41.3% (n= 608) presented glucose abnormalities. Prevalence of prediabetes was 32.9% (95%CI 30.5,35.3%, n= 484) and undiagnosed T2D was 8.4% (95%CI 7.0,9.8%, n= 124). IFG was the most prevalent criteria for the diagnosis of prediabetes (13.8% 95%CI 12.0,15.6%) followed by the combination of IFG + IGT (11.9% 95%CI 10.2,13.5%) and IGT (7.2% 95%CI 5.8,8.4%).

The prevalence of glucose abnormalities increased with age. BMI, central obesity, body fat, insulin resistance and dyslipidemia significantly worsened in PD and undiagnosed T2D groups compared to the normoglycemic group (table I, p<0.05). Total cholesterol and visceral adiposity were significantly higher in PD and undiagnosed T2D, while HDL cholesterol was significantly lower in these groups when compared with normoglycemic patients (PD 41 95%CI 40-42mg/dl, T2D 40 95%CI 38-42mg/dl, NG 44 95%CI 53-46mg/dl, p<0.001). However, these variables were not different between prediabetes and undiagnosed T2D (table I, p ≥0.05). The global prevalence of IR by homeostasis model assessment (HOMA-IR) was 55.7% 95%CI 52.5-58.8%, 41.7% 95%CI 37.5-45.8% in NG, 71.4% 95%CI 66.6-76.1% in PD, and 82.9% 95%CI 74.2-91.5% in undiagnosed T2D, similar to the prevalence of overweight between groups.

Main risk factors associated with PD, when compared to NG were: male sex (OR 2.03 95%CI 1.53,2.70, p<0.001), age > 45 years (OR 1.79 95%CI 1.15,2.78, p 0.009), BMI > 27 kg/m^2 (OR 1.71 95%CI 1.22,2.40, p 0.002), central obesity measured by WC (OR 1.96 95%CI 1.33,2.89, p 0.001), high blood pressure (HBP) (OR 1.54 95%CI 1.02,2.34, p 0.040), family history of T2D (OR 1.42 95%CI 1.04,1.94, p 0.026) and dyslipidemia (OR 2.21 95%CI 1.53,3.20, p<0.001). On the other hand, the main risk factors associated with undiagnosed T2D, when compared to normoglycemia, were male sex, age, overweight, central obesity, HBP, family history of T2D, fetal macrosomy/gestational diabetes, and acanthosis nigricans (all p<0.05, table II). When comparing PD

Table I
CLINICAL AND BIOCHEMICAL CHARACTERISTICS BETWEEN THE STUDY GROUPS

(n= 1 470)	*Groups*			
	NG (n= 862)	*PD (n= 484)*	*nT2D (n= 124)*	*p value (ANOVA)*
Age (years)	37.5 ± 13.0	45.3 ± 12.5*	50.3 ± 10.5*‡	$p< 0.0001$
BMI (kg/m^2)	26.8 ± 5.2	30.2 ± 5.6*	32.2 ± 5.9*‡	$p\leq 0.001$
Waist circumference	86.4 ± 13	95.1 ± 12*	100.2 ± 13*‡	$p< 0.0001$
Body fat (%)	32.2 ± 8.9	35.5 ± 8.5*	38.6 ± 9.0*‡	$p\leq 0.002$
Visceral index (AU)	7.2 ± 6.1	10.8 ± 4.6*	12.0 ± 5.0*	$p< 0.0001$
Fasting glucose (mg/dl)	89 ± 7	104 ± 8*	146 ± 56*‡	$p< 0.0001$
2h_OGTT glucose (mg/dl)	102 ± 20	141 ± 29*	264 ± 83*‡	$p< 0.0001$
HOMA-IR	2.16 ± 1.79	3.45 ± 2.41*	4.89 ± 3.38*‡	$p< 0.0001$
HOMA-IR ≥2.0, n (%)	360 (41.7)	345 (71.4)	103 (82.9)	$p< 0.0001$
Total cholesterol (mg/dl)	180 ± 38	190 ± 39*	193 ± 39*	$p\leq 0.002$
HDL-C (mg/dl)	45 ± 13	41 ± 14*	40 ± 11*	$p\leq 0.003$
Triglycerides (mg/dl)	142 ± 87	178 ± 86*	203 ± 97*‡	$p\leq 0.016$
SBP (mm Hg)	113 ± 14	121 ± 16*	128 ± 19*‡	$p< 0.0001$
Perceived CD risk, n (%)				
Very high	(9.0)	(15.3)	(23.3)	0.003
High	(46.2)	(46.5)	(51.7)	
Low	(39.3)	(32.2)	(21.7)	
Very low	(5.5)	(6.0)	(3.3)	

Data presented as means ± standard deviation.
AU: arbitrary units; BMI: body mass index; CD: chronic disease; HDL-C: high-density lipoprotein cholesterol; NG: normoglycemia; PD: prediabetes; SBP: systolic blood pressure; nT2D: undiagnosed type 2 diabetes; OGTT: oral glucose tolerance test; HOMA-IR: homeostasis model assessment
* $p< 0.05$ v. NG.
‡ $p< 0.05$ vs. PD. Bonferroni post hoc test.

vs. undiagnosed T2D only age, previous gestational diabetes mellitus, and acanthosis nigricans were significantly associated with T2D (all $p<0.05$, table II). No interaction between risk factors were found.

According to ATP III criteria, the prevalence of metabolic syndrome was 48.1% 95%CI 45.3,50.8% among the participants in this study. The most prevalent MetS components were abdominal obesity (69% 95%CI 67.0,71.1) and low HDL-C (64% 95%CI 60.9,66.2), followed by hypertriglyceridemia (43% 95%CI 39.5,45.0), high fasting glucose (33% 95%CI 31.3,36.5), and HBP (32% 95%CI 28.5,33.6). All MetS components were progressively associated with PD and undiagnosed T2D (table III).

Discussion

In this work, we found glucose abnormalities in 41.3% of the studied population, 32.9% with PD, and 8.4% with undiagnosed T2D, as well as a 48.1% prevalence of metabolic syndrome and 55.7% of IR. The main factors associated with T2D and PD were male sex, overweight, central obesity, age family history of T2D, and dyslipidemia.

The prevalence of T2D and PD varies depending on the studied population and the used diagnostic method. Prevalence of undiagnosed T2D using FG has been reported in 2.3 and 1.7% in France,[13,14] 1.13% in Canada,[15] 6.9% in Kuwait,[16] 1.5% in Greece,[17] 5.48% in the Eastern Mediterranean region[18] and 3.96% in Bangladesh;[19] using OGTT, the prevalence of undiagnosed T2D was 8.7% in Sry-Lanka.[20] In Spain using OGTT as a diagnostic test, the prevalence of undiagnosed T2D was 4.3% and risk factors associated with T2D were male sex, obesity, high triglyceride levels, hypertension, family history of T2D, high LDL cholesterol levels, and older age.[21] Here we found a higher prevalence of hyperglycemia and not all the same risk factors associated with PD or T2D, which could be related to a difference in lifestyle. Also in Mexico, using FG and HbA1c during the National Health and Nutrition Survey (Ensanut, in Spanish), the prevalence of undiagnosed T2D was 4.10, 6.38 and 4.55% in 2016, 2018, and 2020, respectively.[1,22]

In a study performed in Texas, USA using OGTT, the global T2D prevalence was 27.6%, and from those, 40% were previously undiagnosed and the main factors associated with T2D were age, obesity, HBP, and triglycerides.[23]

Here we found a prevalence of undiagnosed T2D of 8.4%, which is in agreement whit the high prevalence reported in the Mexican American population, but higher than previously reported by the Ensanut. This difference could be due to the diagnostic tool used to identify T2D since the OGTT could be more useful to identify patients with hyperglycemia than just FG or HbA1c.[24,25] In this study, we are reporting on the highest prevalence of undiagnosed T2D, and this highlights also the high risk of metabolic disturbances in the Latin population and the relevance of these abnormalities in prognosis and mortality in the era of Covid-19, since a great percentage of patients were unaware of hyperglycemia and T2D and by consequence did not have proper metabolic control, affecting prognosis, as previously reported, especially in Mexican population were obesity and T2D have been considered important risk factors for mortality in Covid-19.[26,27] Unfortunately, in Latin American Countries undiagnosed T2D corresponds to 40-50% of the global T2D prevalence, which is different in some other Countries where undiagnosed T2D could be no more than 20% of the global T2D prevalence.[15]

Unfortunately, high prevalence of glucose and metabolic abnormalities is a significant burden on health systems, and it highlights the need for specific diagnostic and therapeutic strategies. It is necessary to reinforce lifestyle interventions in patients with prediabetes and in general population, since lifestyle interventions focused on diet and physical activity have proved to be useful to prevent T2D in patients with prediabetes;[3,9,28-33] together with this, it is important to continue performing research studies with different lifestyle and pharmacological approaches not only to prevent T2D but also to revert prediabetes to normoglycemia,[34] which would be the therapeutic goal

Table II
Association between risk factors and the presence of prediabetes and T2D

(n= 1 470)	*Groups*			*Comparison between groups*		
	NG (n= 862)	*PD (n= 484)*	*T2D (n= 124)*	*PD vs. NG OR95%CI*	*T2D vs. NG OR95%CI*	*T2D vs. PD OR95%CI*
Male sex	263 (30)	212 (44)	42 (34)	OR 2.03 (1.53-2.70) *p*< 0.001	OR 1.78 (1.06-2.99) *p*= 0.028	OR 0.97 (0.60-1.59) *p*= 0.932
Physical inactivity, n (%)	509 (60)	292 (60)	79 (65)	OR 0.94 (0.72-1.23) *p*= 0.719	OR 1.04 (0.63-1.70) *p*= 0.876	OR 1.18 (0.74-1.88) *p*= 0.483
Age (years)				OR 1.02 (1.00-1.04) *p*= 0.022	OR 1.06 (1.03-1.10) *p*< 0.001	OR 1.04 (1.01-1.07) *p*= 0.004
Age > 45 years n (%)	239 (29)	257 (55)	78 (68)	OR 1.79 (1.15-2.78) *p*= 0.009	OR 5.10 (3.11-8.35) *p*<0.001	OR 1.71 (1.07-2.74) *p*= 0.024
BMI > 27 kg/m^2 n (%)	370 (43)	333 (69)	100 (81)	OR 1.71 (1.22-2.40) *p*= 0.002	OR 2.26 (1.20-4.25) *p*= 0.011	OR 1.33 (0.73-2.42) *p*= 0.350
WC (≥90cm M, ≥80cm F)	478 (57)	385 (83)	109 (94)	OR 1.96 (1.33-2.89) *p*= 0.001	OR 3.97 (1.48-10.67) *p*= 0.006	OR 2.10 (0.79-5.57) *p*= 0.132
HBP n (%)	66 (8)	89 (18)	37 (30)	OR 1.54 (1.02-2.34) *p*= 0.040	OR 2.18 (1.23-3.86) *p*= 0.007	OR 1.13 (0.66-1.95) *p*= 0.646
Family history of T2D n (%)	638 (75)	374 (77)	103 (84)	OR 1.42 (1.04-1.94) *p*= 0.026	OR 2.34 (1.27-4.31) *p*= 0.006	OR 1.56 (0.86-2.83) *p*= 0.141
CVD n (%)	14 (2)	10 (2)	5 (4)	OR 0.62 (0.23-1.68) *p*= 0.354	OR 0.84 (0.22-3.17) *p*= 0.800	OR 1.30 (0.38-4.46) *p*= 0.667
FM or GDM n (%)	46 (5)	25 (5)	18 (15)	OR 0.80 (0.45-1.45) *p*= 0.477	OR 2.23 (1.06-4.69) *p*= 0.033	OR 2.21 (1.02-4.76) *p*= 0.042
POS n (%)	35 (4)	24 (5)	6 (5)	OR 1.24 (0.65-2.36) *p*= 0.502	OR 1.35 (0.47-3.89) *p*= 0.569	OR 1.03 (0.36-2.95) *p*= 0.942
Acanthosis nigricans n (%)	75 (9)	51 (11)	25 (20)	OR 1.08 (0.68-1.73) *p*= 0.721	OR 2.99 (1.53-5.82) *p*= 0.001	OR 2.33 (1.23-4.44) *p*= 0.009
Dyslipidemia n (%)	602 (72)	419 (88)	108 (89)	OR 2.21 (1.53-3.20) *p*< 0.001	OR 2.19 (1.14-4.23) *p*= 0.018	OR 0.78 (0.39-1.57) *p*= 0.495

CVD: cardiovascular disease; BMI: body mass index; FM: fetal macrosomia; GDM: gestational diabetes mellitus; HBP: high blood pressure; NG: normoglycemia; PD: prediabetes; POS: polycystic ovary syndrome; T2D: type 2 diabetes.

in patients with prediabetes. Besides that, it is also important to detect as early as possible patients with newly T2D and implement an integral intervention to achieve cardiovascular and metabolic control for prevention of micro and macrovascular complications.[31]

The main risk factors reported associated with T2D are male sex,[21,35] age,[20,21,23,36-38] obesity,[20,21,23,35-38] dyslipidemia,[21,23] family history of T2D,[21,35,36,38] and HBP.[21,23] In our study, the main risk factors associated with T2D in the multivariable analysis and after age adjustment were male sex, family history of T2D, overweight, central obesity, and acanthosis nigricans.

In previous studies, the prevalence of PD has been reported between 2.22-74.7% using FG,[13-19,35-40] and between 11.0-32.0% using OGTT.[20,21,23] In the Mexican-American population, using FG they reported a prevalence of PD of 32%, and they found male sex and family history of T2D as the main risk factors for PD.[35] Also in the Mexican population, in a sample of 384 using FPG and/or HbA1c in a population with at least one T2D risk factor, they found a PD prevalence of 74.7%, being age and obesity as the main risk factors.[37] Other studies in the Mexican population have reported a higher prevalence of PD. In 2008 and 2016 two studies reported a PD prevalence of 43.2 and 44.2% respectively. The differences may be because participants were from different regions in Mexico and because the average age of participants in one of them was close to 60 ages.[41,42]

In our study, we found male sex, age, overweight, central obesity, HBP, family history of T2D, and dyslipidemia as the main risk factors associated with PD and are consistent with previous reports.[35,41-43]

MetS was found in 48.1% of the participants, data consistent with those of Villalpando and colleagues,[44] who described a prevalence of MetS in the Mexican population of 36.8% in 2006 and an increased rate of 0.77 pp/year from 1993 to 2006; with this rate of increase, a prevalence of MetS of 46.6% would be expected, similar to what we found here. Abdominal obesity, low HDL-C, and hyperglyceridemia were the components of MetS with the highest prevalence which is consistent with previous reports.[9] This prevalence was significantly higher in the PD and T2D groups compared to the normoglycemia group, as expected. However, after more than 10 years overweight and obesity together with dyslipidemia and HBP, remain the most prevalent risk factors for cardiometabolic disease in the Mexican population.

Together with the high prevalence of undiagnosed T2D, PD, and MetS, we found a high prevalence of IR, since 55.7% of the whole population had IR, but most alarming, more than 40% of the NG population has already IR, which is in agreement with the high prevalence of metabolic risk factors that have been reported here and through-out previous research works, and the early risk for pancreatic β cell dysfunction in Mexican population with normoglycemia.[9,45]

The findings of the present investigation indicate that most risk factors for T2D are also risk factors for PD, highlighting that conditions leading to the early onset of PD will also result in an early transition to T2D. T2D is one of the most common causes of death in Mexico[28,30] and together with the MetS represents a considerable burden to the Mexican health care system. Unfortunately, in Mexico and around the world, the prevalence of PD and T2D continues to increase, and stopping/reversing this trend should remain a priority and requires multidisciplinary interventions for an early diagnosis and effective treatment strategies. Interestingly, in our study, most of the participants with PD or undiagnosed T2D have the perception of high or very high risk for metabolic diseases, which reflects the patient´s health perception but with low impact on their health care attitude.

With these findings we are highlighting several points: i) prevalence of metabolic abnormalities is high in Mexican population, ii) there is a need for an early identification of these metabolic abnormalities with a

Table III
ASSOCIATION BETWEEN METABOLIC SYNDROME COMPONENTS WITH PD AND UNDIAGNOSED T2D

MetS components	*Groups (n = 1 470)*			*P value**
	NG (n= 862)	*PD (n= 484)*	*T2D (n= 124)*	
HBP ≥ 130/85 mmHg n (%)	192 (22)	204 (42)	74 (60)	p<0.0001
Waist ≥ 90 cm (male) or ≥ 80 cm (female), n (%)	478 (58)	385 (83)	109 (94)	p< 0.0001
Low HDL-C < 40 mg/dl in men, < 50 mg/dl in women, n (%)	482 (59)	330 (70)	86 (75)	p< 0.0001
Blood triglycerides > 150 mg/dl or drug treatment for elevated triglycerides n (%)	273 (32)	267 (55)	84 (70)	p< 0.0001

HBP: high blood pressure; HDL-C: high-density lipoprotein cholesterol; MetS: metabolic syndrome; NG: normoglycemia; PD: prediabetes; T2D: type 2 diabetes.
* Pearson's chi-square.

complete cardio-metabolic risk evaluation, iii) we need to implement public preventive therapeutic strategies to prevent or delay the progression of these metabolic abnormalities, and iv) we should scientifically validate all these diagnostic and therapeutic strategies to make sure they would properly work in our population.

Our study has several limitations; first, it was a cross-sectional design in a limited population from Mexico, which limits understanding of the nature of causality and extrapolation to the whole country; also, the study was performed with a non-random sampling methodology which could affect the representativity of the population, although our participants share many similarities with previous health surveys performed in Mexico.[9] Main strength of our study is that all participants were diagnosed by OGTT, which has been considered as one of the gold standard to identify glucose abnormalities and allows an integrative approach regarding glucose metabolism and a more precise prevalence measurement, since FG or HbA1c could underestimate the real prevalence of glucose abnormalities and refers only to a specific type of abnormality, as previously reported.[46]

We conclude that prevalence of PD, T2D, insulin resistance and metabolic syndrome is high in population from Guanajuato, Mexico and this is related to a high prevalence of risk factors presents in our population. More programs designed to an early diagnosis and treatment of these abnormalities are required in Mexican population and around the world.

Acknowledgments

We thank all the participants for your participation in the study, and the personnel from the Metabolic Research Laboratory.

Funding

Part of this work was performed thanks to the financial support assigned to RGM by the University of Guanajuato through the *Convocatoria Institucional para Fortalecer la Excelencia Académica 2014 y 2015*.

Declaration of conflict of interests. The authors declare that they have no conflict of interests.

References

1. Basto-Abreu AC, López-Olmedo N, Rojas-Martínez R, Aguilar-Salinas CA, De la Cruz-Góngora V, Rivera-Dommarco J, *et al*. Prevalence of diabetes and glycemic control in Mexico: national results from 2018 and 2020. Salud Publica Mex. 2021;63(6):725-33. https://doi.org/10.21149/12842

2. Rull JA, Aguilar-Salinas CA, Rojas R, Rios-Torres JM, Gómez-Pérez FJ, Olaiz G. Epidemiology of type 2 diabetes in Mexico. Arch Med Res. 2005;36(3):188-96. https://doi.org/10.1016/j.arcmed.2005.01.006

3. Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurstova K, Duncan BB, *et al*. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Res Clin Pract. 2022;183:109119. https://doi.org/10.1016/j.diabres.2021.109119

4. Ferrannini E, Gastaldelli A, Iozzo P. Pathophysiology of prediabetes. Med Clin North Am. 2011;95(2):327-39. https://doi.org/10.1016/j.mcna.2010.11.005

5. Ogurtsova K, Guariguata L, Barengo NC, Lopez-Doriga-Ruiz P, Sacre W, Karuranga S, *et al*. IDF diabetes Atlas: Global estimates of undiagnosed diabetes in adults for 2021. Diabetes Res Clin Pract. 2022;183:109118. https://doi.org/10.1016/j.diabres.2021.109118

6. Urena-Bogarin EL, Martínez-Ramírez HR, Torres-Sánchez JR, Hernández-Herrera A, Cortés-Sanabrina L, Cueto-Mnazano A. Prevalence of pre-diabetes in young Mexican adults in primary health care. Fam Pract. 2015;32(2):159-64. https://doi.org/10.1093/fampra/cmu047

7. American Diabetes Association Professsional Practice Committee. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2022. Diabetes Care. 2022;45(suppl 1):S17-38. https://doi.org/10.2337/dc22-S002

8. Alberti KG, Eckel RH, Groundy SM, Zimmet PZ, Cleeman JI, Donato KA, *et al*. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation. 2009;120(16):1640-5. https://doi.org/10.1161/CIRCULATIONAHA.109.192644

9. Rojas-Martinez R, Aguilar-Salinas CA, Romero-Martínez M, Castro-Porras L, Gómez-Velasco D, Mehta R. Trends in the prevalence of metabolic syndrome and its components in Mexican adults, 2006-2018. Salud Publica Mex. 2021;63(6):713-24. https://doi.org/10.21149/12835

10. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia. 1985;28:412-9. https://doi.org/10.1007/BF00280883

11. Gayoso-Diz P, Otero-González A, Rodriguez-Alvarez MX, Gude F, García F, De Francisco A, *et al*. Insulin resistance (HOMA-IR) cut-off values and the metabolic syndrome in a general adult population: effect of gender and age: EPIRCE cross-sectional study. BMC Endocr Disord. 2013;13. https://doi.org/10.1186/1472-6823-13-47

12. Basto-Abreu A, López-Olmedo N, Rojas-Martínez R, Aguilar-Salinas CA, Moreno-Banda GL, Carnalla M, *et al*. Prevalencia de prediabetes y diabetes en México: Ensanut 2022. Salud Publica Mex. 2023;65(suppl 1):s163-8. https://doi.org/10.21149/14832

13. Hauguel-Moreau M, Hergault H, Cazabat L, Pépin M, Beauchet A, Aidan V, *et al*. Prevalence of prediabetes and undiagnosed diabetes in a large urban middle-aged population: the CARVAR 92 cohort. Cardiovasc Diabetol 2023;22(31). https://doi.org/10.1186/s12933-023-01761-3

14. Lailler G, Piffaretti C, Fuentes S, Nabe HD, Oleko A, Cosson E, *et al*. Prevalence of prediabetes and undiagnosed type 2 diabetes in France: Results from the national survey ESTEBAN, 2014-2016. Diabetes Res Clin Pract. 2020;165:108252. https://doi.org/10.1016/j.diabres.2020.108252

15. Rosella LC, Lebenbaum M, Fitzpatrick T, Zuk A, Booth GL. Prevalence of prediabetes and undiagnosed diabetes in Canada (2007-2011) according to fasting plasma glucose and HbA1c screening criteria. Diabetes Care. 2015;38(7):1299-305 https://doi.org/10.2337/dc14-2474

16. Mohammad A, Ziyab AH, Mohammad T. Prevalence of prediabetes and undiagnosed diabetes among Kuwaiti adults: a cross-sectional study. Diabetes Metab Syndr Obes. 2021;14:2167-76. https://doi.org/10.2147/DMSO.S296848

17. Makrilakis K, Kalpourtzi N, Ioannidis I, Iraklianou S, Raptis A, Sotiropoulos A, *et al*. Prevalence of diabetes and pre-diabetes in Greece. Re-

sults of the First National Survey of Morbidity and Risk Factors (EMENO) study. Diabetes Res Clin Pract. 2021;172:108646. https://doi.org/10.1016/j.diabres.2020.108646
18. Mirahmadizadeh A, Fathalipour M, Mokhtari AM, Zeighami S, Hassanipour S, Heiran A. The prevalence of undiagnosed type 2 diabetes and prediabetes in Eastern Mediterranean region (EMRO): A systematic review and meta-analysis. Diabetes Res Clin Pract. 2020;160:107931. https://doi.org/10.1016/j.diabres.2019.107931
19. Islam FM, Chakrabarti R, Islam MT, Wahab M, Lamoureux E, Finger RP, *et al*. Prediabetes, diagnosed and undiagnosed diabetes, their risk factors and association with knowledge of diabetes in rural Bangladesh: The Bangladesh Population-based Diabetes and Eye Study. J Diabetes. 2016;8(2):260-8. https://doi.org/10.1111/1753-0407.12294
20. Rannan-Eliya RP, Wijemunige N, Perera P, Kapuge Y, Gunawardana N, Sigera C, *et al*. Prevalence of diabetes and pre-diabetes in Sri Lanka: a new global hotspot-estimates from the Sri Lanka Health and Ageing Survey 2018/2019. BMJ Open Diabetes Res Care. 2023;11(1):e003160. https://doi.org/10.1136/bmjdrc-2022-003160
21. Aguayo A, Urrutia I, González-Frutos T, Martínez R, Martínez-Indart L, Castaño L, *et al*. Prevalence of diabetes mellitus and impaired glucose metabolism in the adult population of the Basque Country, Spain. Diabet Med. 2017;34(5):662-6. https://doi.org/10.1111/dme.13181
22. Basto-Abreu A, Barrientos-Gutiérrez T, Rojas-Martínez R, Aguilar-Salinas CA, López-Olmedo N, De la Cruz-Góngora V, *et al*. Prevalence of diabetes and poor glycemic control in Mexico: results from Ensanut 2016. Salud Publica Mex. 2020;62(1):50-9. https://doi.org/10.21149/10752
23. Fisher-Hoch SP, Vatcheva KP, Rahbar MH, McCormick JB. Undiagnosed diabetes and pre-diabetes in health disparities. PLoS One. 2015;10(7):e01331. https://doi.org/10.1371/journal.pone.0133135
24. Hellgren M, Hjorleifsdottir-Steiner K, Bennet L. Haemoglobin A1c as a screening tool for type 2 diabetes and prediabetes in populations of Swedish and Middle-East ancestry. Prim Care Diabetes. 2017;11(4):337-43. https://doi.org/10.1016/j.pcd.2017.04.008
25. Thewjitcharoen Y, Elizabeth AJ, Butadej S, Nakasatien S, Chotwanvirat P, Wanothayaroj E, *et al*. Performance of HbA1c versus oral glucose tolerance test (OGTT) as a screening tool to diagnose dysglycemic status in high-risk Thai patients. BMC Endocr Disord. 2019;19(23). https://doi.org/10.1186/s12902-019-0339-6
26. Sardu C, D'Onofrio N, Balestrieri ML, Barbieri M, Rizzo MR, Messina V, *et al*. Outcomes in patients with hyperglycemia affected by COVID-19: can we do more on glycemic control? Diabetes Care. 2020;43(7):1408-15. https://doi.org/10.2337/dc20-0723
27. Bello-Chavolla OY, Bahena-López JP, Antonio-Villa NE, Vargas-Vázquez A, González-Díaz A, Márquez-Salinas A, *et al*. Predicting mortality due to SARS-CoV-2: a mechanistic score relating obesity and diabetes to COVID-19 outcomes in Mexico. J Clin Endocrinol Metab. 2020;105(8):2752-61. https://doi.org/10.1210/clinem/dgaa346
28. Alegre-Diaz J, Herrington W, López-Cervantes M, Gnatiuc L, Ramirez R, Hill M, *et al*. Diabetes and cause-specific mortality in Mexico City. N Engl J Med. 2016;375:1961-71. https://doi.org/10.1056/NEJMoa1605368
29. Aroda VR, Knowler WC, Crandall JP, Perreault L, Edelstein SL, Jeffries SL, *et al.* Metformin for diabetes prevention: insights gained from the Diabetes Prevention Program/Diabetes Prevention Program Outcomes Study. Diabetologia. 2017;60:1601-11. https://doi.org/10.1007/s00125-017-4361-9
30. Bello-Chavolla OY, Antonio-Villa NE, Fermín-Martínez CA, Fernández-Chirino L, Vargas-Vázquez A, Ramírez-García D, *et al*. Diabetes-related excess mortality in Mexico: a comparative analysis of national death registries between 2017-2019 and 2020. Diabetes Care. 2022;45(12):2957-66. https://doi.org/10.2337/dc22-0616
31. Gong Q, Zhang P, Wang J, Ma J, An Y, Chen Y, *et al*. Morbidity and mortality after lifestyle intervention for people with impaired glucose tolerance: 30-year results of the Da Qing Diabetes Prevention Outcome Study. Lancet Diabetes Endocrinol. 2019;7(6):452-61. https://doi.org/10.1016/S2213-8587(19)30093-2
32. Guardado-Mendoza R, García-Magaña MA, Martínez-Navarro LJ, Macías-Cervantes HE, Aguilar-Guerrero R, Suárez-Pérez EL, *et al*. Effect of linagliptin plus insulin in comparison to insulin alone on metabolic control and prognosis in hospitalized patients with SARS-CoV-2 infection. Sci Rep. 2022;12:536. https://doi.org/10.1038/s41598-021-04511-1
33. Guardado-Mendoza R, Salazar-López SS, Álvarez-Canales M, Farfán-Vázquez D, Martínez-López YE, Jiménez-Ceja LM, *et al*. The combination of linagliptin, metformin and lifestyle modification to prevent type 2 diabetes (PRELLIM). A randomized clinical trial. Metabolism. 2020;104:154054. https://doi.org/10.1016/j.metabol.2019.154054
34. Sandforth A, von Schwartzenberg R, Vazquez-Arreola E, Hanson RL, Sancar G, Katzenstein S, *et al*. Mechanisms of weight loss-induced remission in people with prediabetes: a post-hoc analysis of the randomised, controlled, multicentre Prediabetes Lifestyle Intervention Study (PLIS). Lancet Diabetes Endocrinol. 2023;11(11):798-810. https://doi.org/10.1016/S2213-8587(23)00235-8
35. Vatcheva KP, Fisher-Hoch SP, Reininger BM, McCormick JB. Sex and age differences in prevalence and risk factors for prediabetes in Mexican-Americans. Diabetes Res Clin Pract. 2020;159:107950. https://doi.org/10.1016/j.diabres.2019.107950
36. Moradpour F, Rezei S, Piroozi B, Moradi G, Moradi Y, Piri N, *et al*. Prevalence of prediabetes, diabetes, diabetes awareness, treatment, and its socioeconomic inequality in west of Iran. Sci Rep. 2022;12:17892. https://doi.org/10.1038/s41598-022-22779-9
37. Villanueva-Sosa LG, Cordero-Franco HF, Salinas-Martinez AM. Prevalence of prediabetes based on fasting plasma glucose and glycosylated hemoglobin in an at-risk Mexican population. Metab Syndr Relat Disord. 2015;13(8):352-5. https://doi.org/10.1089/met.2015.0040
38. Xia M, Liu K, Feng J, Zheng Z, Xie X. Prevalence and risk factors of type 2 diabetes and prediabetes among 53,288 middle-aged and elderly adults in China: a cross-sectional study. Diabetes Metab Syndr Obes. 2021;14:1975-85. https://doi.org/10.2147/DMSO.S305919
39. Akhtar S, Nasir JA, Ali A, Asghar M, Majeed R, Sarwar A. Prevalence of type-2 diabetes and prediabetes in Malaysia: A systematic review and meta-analysis. PLoS One. 2022;17:e0263139. https://doi.org/10.1371/journal.pone.0263139
40. Broz J, Malinovská J, Nunes K, Kucera K, Rožeková K, Žejglicová K, *et al*. Prevalence of diabetes and prediabetes and its risk factors in adults aged 25-64 in the Czech Republic: A cross-sectional study. Diabetes Res Clin Pract. 2020;170:108470. https://doi.org/10.1016/j.diabres.2020.108470
41. Guerrero-Romero F, Rodríguez-Morán M, Pérez-Fuentes R, Sánches-Guillén MC, González-Ortiz M, Martínez-Abundis E, *et al*. Prediabetes and its relationship with obesity in Mexican adults: The Mexican Diabetes Prevention (MexDiab) Study. Metab Syndr Relat Disord. 2008;6(1):15-23. https://doi.org/10.1089/met.2007.0020
42. Kumar A, Wong R, Ottenbacher KJ, Al Snih S. Prediabetes, undiagnosed diabetes, and diabetes among Mexican adults: findings from the Mexican Health and Aging Study. Ann Epidemiol. 2016;26(3):163-70. https://doi.org/10.1016/j.annepidem.2015.12.006
43. Menon VU, Kumar KV, Gilchrist A, Sugathan TN, Sundaram KR, Nair V, *et al*. Prevalence of known and undetected diabetes and associated risk factors in central Kerala--ADEPS. Diabetes Res Clin Pract. 2006;74(3):289-94. https://doi.org/10.1016/j.diabres.2006.03.025
44. Villalpando S, Shamah-Levy T, Rojas R, Aguilar-Salinas CA. Trends for type 2 diabetes and other cardiovascular risk factors in Mexico from 1993-2006. Salud Publica Mex. 2010;52(suppl 1):S72-9. https://doi.org/10.1590/s0036-36342010000700011
45. Vilchis-Flores LH, Barajas-Medina GA, Villa-Martínez AK, Salazar-López SS, Luna-Patiño GA, Quiroz-Hernández ME, *et al*. Pancreatic beta-cell dysfunction in normoglycemic patients and risk factors. Acta Diabetol. 2019;56:1305-14. https://doi.org/10.1007/s00592-019-01411-9
46. Barry E, Roberts S, Oke J, Vijayaraghavan S, Normansell R, Greenhalgh T. Efficacy and effectiveness of screen and treat policies in prevention of type 2 diabetes: systematic review and meta-analysis of screening tests and interventions. BMJ. 2017;356:i6538. https://doi.org/10.1136/bmj.i6538