Type II diabetes mellitus and menopause: a multinational study

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Key words: TYPE II DIABETES, MENOPAUSE, CLIMACTERIC SYMPTOMS, BLOOD PRESSURE, LATIN AMERICA

ABSTRACT

Background Type II diabetes mellitus causes metabolic changes that may lead to early menopause and worsen climacteric symptoms.

Objectives To determine the risk factors for type II diabetes mellitus and assess the impact of this disease on the age of menopause and on climacteric symptoms.

Methods A total of 6079 women aged between 40 and 59 years from 11 Latin American countries were requested to answer the Menopause Rating Scale and Goldberg Anxiety-Depression Scale.

Results The prevalence of diabetes was 6.7%. Diabetes mellitus was associated with arterial hypertension (odds ratio (OR) 4.49; 95% confidence interval (CI) 3.47–5.31), the use of psychotropic drugs (OR 1.54; 95% CI 1.22–1.94), hormonal therapy (OR 1.46; 95% CI 1.11–1.92), $\geq$50 years of age (OR 1.48; 95% CI 1.17–1.86), overweight or obese (OR 1.47; 95% CI 1.15–1.89), and waist circumference $\geq$88 cm (OR 1.32; 95% CI 1.06–1.65). Factors associated with lower risk of diabetes were the use of hormonal contraceptives (OR 0.55; 95% CI 0.35–0.87), alcohol (OR 0.73; 95% CI 0.54–0.98) and living in cities $>$2500 meters above sea level (OR 0.70; 95% CI 0.53–0.91) or with high temperatures (OR 0.67; 95% CI 0.51–0.88). In turn, diabetes tripled the risk of menopause in women under 45 years of age. Diabetes did not increase the risk of deterioration of quality of life due to climacteric symptoms.

Conclusion Menopause does not increase the risk of type II diabetes mellitus. Diabetes is associated with early menopause in women under 45 years of age.

INTRODUCTION

In most countries in recent decades, economic development and changes in lifestyle have increased longevity and the number of people who are overweight or obese. These changes have increased significantly the prevalence of diabetes mellitus, especially type II diabetes (DM-II). In 2000, 171 million people were estimated to have diabetes around the world, and this figure is expected to rise to 366 million by 2030[1].

DM-II is very important in women since it is one of the most common chronic diseases in postmenopausal women and it is an underlying factor for cardiovascular diseases, which is the main cause of death in Western societies[2]. Additionally, DM-II is associated with an increase in breast cancer, which is a disease with high prevalence in older women. A meta-analysis showed 23% higher risk of breast cancer in diabetic women[3]. Also, DM-II accounts for a higher proportion of deaths in women than in men[4].

Menopause has been associated with an increase in abdominal fat caused by the depletion of ovarian function[5]. These changes in body composition may cause disturbances in insulin sensitivity and in glucose metabolism in postmenopausal women[6]. Menopause is a relevant physiological event in a woman's life and, because of the biological and psychosocial changes that it causes, it may impact on the risk of diabetes; however, few studies have evaluated the effect of diabetes on the age of menopause and on climacteric

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ORIGINAL ARTICLE

DOI: 10.3109/13697137.2013.798272

Received 25-03-2013
Revised 15-04-2013
Accepted 18-04-2013

symptomatology. Some authors have suggested that menopause can increase the risk of diabetes[7], but this is controversial[6]. Hormone replacement therapy (HRT) in postmenopause improves the metabolic control of women with DM-II and/or decreases the prevalence of diabetes; therefore, a protective role of ovarian steroids on the risk of diabetes has been suggested[8].

There are few studies that analyze the relationship between DM-II and menopause. The analysis is complicated since each of these two conditions has multiple interacting variables, which may modulate the clinical expression[9]. The objective of this study was to determine the risk factors for DM-II and assess the impact of this disease on the age of menopause and on climacteric symptoms.

MATERIALS AND METHODS

Participants

A large cross-sectional study was carried out on women between the ages of 40 and 59 years, in health centers of cities with populations $>500\,000$ inhabitants in 11 Latin American countries. The inclusion criteria were Hispanic women with normal health who were companions of patients who consulted in medical centers. According to the National Center for Health Statistics, normal health refers to being able to perform routine activities[10]. Women were excluded if they were black and indigenous, or presented mental disorders so that they could not fill in the form, or had psychic or physical disabilities which could hinder the process of the interview. Women fulfilling the inclusion criteria were requested to complete the questionnaire. Informed consent was obtained prior to the implementation of the survey, according to the Declaration of Helsinki[11]. The research protocol of this study was reviewed and approved by the Bioethics Committee of the PROSAM Foundation, Santiago de Chile, Chile. Using statistical software (EPI-INFO 6.04, Centers for Disease Control and Prevention, Atlanta, USA, 2001), a small sample size was calculated as 196 women per center by considering that each center covered an estimated population of 50 000 women[12] and assuming that 9% of the surveyed population would suffer DM-II[13] with an estimated 5% error and a 95% confidence interval. At least 250 respondents were requested from each center.

Tools

General data

To record the data, an itemized questionnaire was previously constructed and validated with 50 women before the implementation at the Latin American centers affiliated to the Collaborative Group for Research of the Climacteric in Latin America (REDLINC) participating in this study; the so-called REDLINC V.

Study variables

Data were collected on age, educational level (years of schooling), parity, menopausal status, years of postmenopause, surgical menopause and marital status and/or if currently they have a partner. In addition, lifestyle and other personal factors, i.e. smoking, alcohol consumption and physical activity, were included in the data. Medical care, drug use, background of chronic diseases, psychiatric attention as well as the use of psychotropic drugs and hormone therapy/alternative therapies for menopause or contraceptives were assessed. Each group was assigned a REDLINC center number (city and country).

Definition of variables

Insufficient educational level was considered to be 12 years of schooling or less[14]. Menopausal status definitions were based on STRAW[15]: premenopausal (women having regular menses); perimenopause (irregular menses >7 days from their normal cycle); early postmenopause (1–4 years); and late postmenopause (≥ 5 years). Premenopausal women were divided into two groups: those who were older and those younger than 45 years of age. Other characteristics were defined as: current smoking: $\geq$ one cigarette per day; alcohol: $\geq$ one drink weekly; obesity: body mass index (BMI) ≥ 30 kg/m^2; abdominal obesity with waist circumference ≥ 88 cm; hypertension: blood pressure $\geq 140/90$ mmHg or antihypertensive therapy and diabetes mellitus; medical diagnosis (glycemia >125 mg/dl at two times) or use of hypoglycemic drugs. Cities with altitudes >2500 m were considered as high cities and those with average maximum temperatures >30°C were considered as hot cities.

Menopause Rating Scale

The Menopause Rating Scale (MRS)[16] is a questionnaire that assesses the presence and intensity of 11 climacteric symptoms. It is divided into three subscales: (1) Somatic: hot flushes, heart discomfort, sleep problems, muscle problems and joint problems; (2) Psychological: depressive mood, irritability, anxiety and physical and mental exhaustion; and (3) Urogenital: sexual problems, bladder problems, and vaginal dryness. The respondent provides her personal perception by checking one of five possible boxes of 'severity' for each of the items from 0 to 4 (0, no complaints; 1, mild; 2, moderate; 3, severe; 4, extremely severe symptoms). The composite scores for each of the domains are obtained by adding up the scores for the individual items in the respective domains. The higher the score, the more increased the deterioration of the quality of life of the respondent. If the total score is higher than 16 points, there is a severe impairment in the quality of life. This questionnaire has been translated into 27 languages and validated in several Spanish-speaking countries[17,18].

Goldberg Anxiety and Depression Scale

The Goldberg Anxiety and Depression Scale (GADS)[19] for the diagnosis of anxiety or depression also differentiates between

them and their respective intensities. The GADS has two subscales each with nine yes–no questions: anxiety (questions 1–9) and depression (questions 10–18). It has been validated in Spanish by Montón and colleagues[20].

Statistical analysis

Data analysis was performed using the EPI-INFO statistical program (Version 3.5.1 2008, Centers for Disease Control and Prevention, Atlanta, GA, USA; WHO, Basel, Switzerland). The results were presented as mean ± standard deviation (SD) and percentages (95% confidence interval, CI). The Kolmogorov–Smirnov test was used to assess the normality of data distribution; the Bartlett test was used to evaluate the homogeneity of measured variance. According to this group, comparisons were performed with the Student's *t*-test (means), analysis of variance (several continuous data) or the Mann–Whitney test (non-parametric data). Percentages between groups were evaluated with the χ^2 test. A p value of <0.05 was considered as statistically significant.

Two models of logistic regression analysis were performed for the simultaneous assessment of several variables influencing the presence of DM-II or menopause (dependent variable). Independent variables to be entered in the regression model were as follows: depression/anxiety, Goldberg (yes/no), current smoking (yes/no), alcohol (yes/no), obesity (yes/no), arterial hypertension (yes/no), diabetes mellitus (yes/no), older age (yes $\geq$50 years, median), postmenopause status (yes/no), surgical menopause (yes/no), vasomotor symptoms (yes/no), medication use (contraceptives, HRT for the menopause, psychotropic drugs), having a stable partner (yes/no), and low level of schooling ($\leq$12 years, yes). Entry of variables into the model was considered with a 5% significance level and the stepwise procedure performed. Interactions between significant variables found during regression model construction were also considered for the final model. Adequacy of the regression model was demonstrated with the Hosmer–Lemeshow goodness-of-fit test.

RESULTS

The refusal rate for study participation was 7.9%, leaving 6079 surveys for analysis. The general characteristics of all studied women are given in Table 1. The study found that 410 women (6.7%) were diabetic. The mean age was 49.7 ± 5.4 years and the average length of schooling was 10.8 ± 4.9 years. A relatively high percentage (36.8%) lived in cities located at 2500 m above sea level and with temperatures over 30°C (40.5%); 68.9% of the women had a stable partner, and the average number of children was 2.6 ± 1.6. More than half (57.6%) were in postmenopause and 13.2% were using HRT; 11.3% were smokers, and 17.4% drank at least one alcoholic drink per week. Anxiety and depression affected half of the women and about 20% used psychotropic drugs or were obese, sedentary and hypertensive. More than half of the respondents were considered to be in good health.

Table 1 Epidemiological characteristics of diabetic and non-diabetic women. Data are presented as means ± standard deviations or percentages

	All (n = 6079)	*Non-diabetic* (n = 5669)	*Diabetic* (n = 410)	*p Value*
Age (years)	49.7 ± 5.4	49.7 ± 5.4	52.0 ± 5.4	<0.0001*
Years of study	10.8 ± 4.9	10.8 ± 4.9	10.8 ± 5.0	ns*
Living at high altitude (≥2500 m)	36.8	37.2	30.5	<0.006†
Living in hot cities (>30°C)	40.5	40.7	36.6	ns†
Living with a stable partner	68.9	68.6	72.2	ns†
Parity	2.6 ± 1.6	2.5 ± 1.5	2.9 ± 1.7	<0.0001†
Postmenopausal	57.6	56.4	73.9	<0.0001†
Median menopause age (years)	49.8	50.1	48.5	
Hormone therapy use	13.2	12.6	21.2	<0.0001†
Current smoker	11.3	11.3	11.0	ns†
Alcohol (≥1 drink weekly)	17.4	19.7	14.4	ns†
Anxiety (Goldberg)	59.7	59.3	65.6	<0.01†
Depression (Goldberg)	46.5	45.9	55.1	<0.0002†
Psychotropic drug use	20.4	19.5	31.7	<0.0001†
Obesity (BMI≥30 kg/m^2)	18.5	17.9	28.0	<0.0001†
Waist circumference ≥88 cm	40.0	39.0	53.4	<0.0001†
Physical activity (30 min/4 times/week)	19.5	19.5	18.5	ns†
Hypertension	22.9	20.4	56.8	<0.0001†
Good health (self-perception)	55.1	55.9	44.4	<0.0001†

*, Student's *t*-test; †, χ^2 test

BMI, body mass index; ns, non-significant

Table 1 shows that diabetic women have different characteristics when compared to non-diabetic women. They are older (52.0 ± 5.4 vs. 49.7 ± 5.4 years, $p < 0.0001$), a minor number of them live in cities located >2500 m above sea level (30.5% vs. 37.2%, $p < 0.006$), have a higher parity (2.9 ± 1.7 vs. 2.5 ± 1.5 children, $p < 0.001$), their average menopause age is lower (48.4 vs. 50.1 years of age) and they use HT more frequently (21.2% vs. 12.6%, $p < 0.001$). Moreover, diabetic women experience more anxiety, depression, and psychotropic drug use, greater obesity, larger waist circumference and greater arterial hypertension. In general, diabetic women have a poorer perception of their health.

Table 2 presents the prevalence of diabetes and the odds ratios of different variables observed with more prevalence in the diabetic women in Table 1. Age only begins to increase the risk from 50 to 54 years of age (OR 1.76; 95% CI 1.23–2.53), and the risk strongly increases during the quinquennium of 55–59 years (OR 3.03; 95% CI 2.15–4.30). Being overweight involves a significant increase in the risk (OR 1.74; 95% CI 1.35–2.25), and in obese women this increase is even higher (OR 2.43; 95% CI 1.82–3.23). A waist circumference >88 cm has a risk equivalent to being overweight (OR 1.79; 95% CI 1.46–2.21). The main risk factor found during this study was arterial hypertension (OR 5.13; 95% CI 4.14–6.35). Early menopause implicates an increased risk of DM-II (OR 1.85; 95% CI 1.16–2.97); such risk increases in the late postmenopause (OR 3.39; 95% CI 2.17–5.35). Surgical menopause and the use of HRT seemed to pose a significant risk of diabetes. On the other hand, the use of oral contraceptives was associated with a lower risk (OR 0.42; 95% CI 0.26–0.66), the same as living in cities located at >2500 m above sea level (OR 0.74; 95% CI 0.59–0.93). Depression, anxiety and the use of psychoactive drugs were associated with increased risk of diabetes.

Table 3 presents the model of logistic regression where arterial hypertension is the strongest variable associated with the risk of DM-II (OR 4.29; 95% CI 3.47–5.31). Postmenopause adjusted only by age was still a risk factor for diabetes (OR 1.54; 95% CI 1.15–2.05), but, when the variables of Table 3 were included in the model, this association disappeared.

Table 4 shows the percentage of women with natural menopause at different ages according to the absence or presence of DM-II. In the age range of 40–44 years, just 13.2% of non-diabetic women had experienced natural menopause; this percentage increases to 29.5% in diabetic women of the same age. The risk of postmenopause in diabetic women of 40–44 years of age increases almost three times (OR 2.76; 95% CI 1.32–5.67). After adjusting related confounding factors, the OR did not change significantly within that group of women (OR 2.71; 95% CI 1.38–5.34). On the other hand, in women >45 years of age, diabetes was not associated with a greater risk of becoming postmenopausal.

Table 5 presents the 11 climacteric symptoms assessed by the MRS in diabetic and normal women. Diabetic women have more risk of experiencing associated sleep problems (OR 1.51; 95% CI 1.20–1.90), joint/muscular discomfort (OR 1.42; 95% CI 1.13–1.80), anxiety (OR 1.31; 95% CI 1.06–1.61), physical/mental exhaustion (OR 1.54; 95% CI 1.21–1.98) and genitourinary symptoms. The risk of having impaired quality of life in diabetic women due to climacteric symptoms is 34% higher than in non-diabetic women (OR 1.34; 95% CI 1.02–1.778). Nevertheless, in a model of logistic regression, after adjusting for age, menopause, use of HRT, oral contraceptives and psychotropic drugs, obesity, physical activity, years of schooling, smoking, altitude and temperature of the cities where the women live, DM-II was not associated with deterioration in the quality of life due to a higher climacteric symptomatology (OR 1.05; 95% CI 0.79–1.38).

Table 6 presents the results obtained with GADS. Diabetic women felt that they had slowed up, lost interest in things and felt worse in the morning ($p < 0.005$) in most of the depression items. They also reported to have been sleeping poorly, to have been more worried about their health, to have had headaches or neck aches and to have had more difficulty falling asleep than other women in this study ($p < 0.005$).

DISCUSSION

The International Diabetes Federation (IDF) reported that 366 million people had diabetes in 2011, and that by 2030 this will have risen to 552 million. The number of people with type 2 diabetes is increasing in every country. The majority of people with diabetes are between 40 and 59 years of age. In 2011, 4.4% of the adult world-wide population had diabetes. The estimated global prevalence was 8.3% in 2011[21]. The prevalence rate of 3.1% for the Western Pacific Region is significantly lower than the 7.9% in the North American area and 7.8% in the European Region. In Latin America, the IDF estimated a prevalence of 5.5%. The percentage found in this study was 6.7%, which agrees with the estimates of the IDF, even though these were made a decade ago. The IDF calculated that, for the year 2025, the prevalence of diabetes in the world will reach 6.3%. By the same date, more than 7% of the adult population of Latin America will have diabetes.

When comparing the epidemiological characteristics of diabetic women with those of normal women, this study found a number of differences related to age, weight, menopause, etc., but, when a logistic regression was performed, the association continued for only a few variables. Hypertension in the logistic regression is the main risk factor for DM-II and it quadruples the risk in this group of Latin American women. Progetto Menopausa Italia, a study of more than 40 000 women with climacteric symptoms, places arterial hypertension within the main risk factors of diabetes with an OR of 3.03 (95% CI 2.62–3.31)[22]. Another study, representative of all Mexico, studied 45 000 individuals of both sexes >20 years of age and also found that hypertension is a significant risk factor for diabetes in both sexes, but especially for women[23]. It is not surprising that hypertension is also

Table 2 Variables associated with risk of type II diabetes in middle-aged women

Variables	*Total number of women*	*Percentage of women with diabetes (95% confidence interval)*	*Odds ratio (95% confidence interval)*
Age (years)			
40–44	1175	4.1 (3.1–5.4)	1.00
45–49	1692	4.3 (3.4–5.4)	1.06 (0.72–1.57)
50–54	1761	7.0 (5.9–8.3)	1.76 (1.23–2.53)
55–59	1451	11.4 (9.9–13.2)	3.03 (2.15–4.30)
Body mass index (kg/m^2)			
<18.5	113	1.8 (0.2–6.2)	0.38 (0.06–1.63)
18.5–24.9	2248	4.5 (3.7–5.4)	1.00
25–29.9	2491	7.5 (6.6–8.7)	1.74 (1.35–2.25)
≥ 30	1127	10.2 (8.5–12.2)	2.43 (1.82–3.23)
Waist circumference ≥ 88 *cm*			
No	3649	5.2 (4.5–6.0)	1.00
Yes	2430	9.0 (7.9–10.2)	1.79 (1.46–2.21)
Arterial hypertension			
No	4668	3.8 (3.3–4.4)	1.00
Yes	1391	16.8 (14.8–18.8)	5.13 (4.14–6.35)
Menopausal status			
Premenopause, 40–44 years	711	3.5 (2.3–5.2)	1.00
Premenopause, ≥ 45 years	949	4.8 (3.6–6.5)	1.40 (0.82–2.38)
Perimenopause	916	3.9 (2.8–5.5)	1.12 (0.65–1.96)
Early postmenopause (<5years)	1758	6.3 (5.2–7.6)	1.85 (1.16–2.97)
Late postmenopause (≥ 5 years)	1745	11.0 (9.6–12.6)	3.39 (2.17–5.35)
Surgical menopause			
No	5120	6.1 (5.4–6.8)	1.0
Yes	959	10.3 (8.5–12.5)	1.78 (1.39–2.28)
Hormonal therapy			
No	5275	6.1 (5.5–6.8)	1.00
Yes	804	10.8 (8.8–13.2)	1.86 (1.43–2.41)
Hormonal contraceptive			
No	5378	7.2 (6.5–7.8)	1.00
Yes	701	3.1 (2.0–4.8)	0.42 (0.26–0.66)
Living at high altitude (≥ 2500 m)			
No	3844	7.4 (6.6–8.3)	1.00
yes	2235	5.6 (4.7–6.6)	0.74 (0.59–0.93)
Living in hot cities (≥ 30°C)			
No	3620	7.2 (6.4–8.1)	1.00
Yes	2459	6.1 (5.2–7.1)	0.84 (0.68–1.04)
Anxiety (Goldberg)			
No	2451	5.8 (4.9–6.8)	1.00
Yes	3628	7.4 (6.6–8.3)	1.31 (1.06–1.63)
Depression (Goldberg)			
No	3523	5.7 (4.9–6.5)	1.00
Yes	2826	8.0 (7.0–9.1)	1.45 (1.18–1.79)
Psychotropic drug use			
No	4841	5.8 (5.2–6.5)	1.00
Yes	1238	10.5 (8.9–12.4)	1.91 (1.52–2.40)

Table 3 Risk factors related to type II diabetes: logistic regression analysis. Variables removed from the model: depression (Goldberg), anxiety (Goldberg), smoking, postmenopause, surgical menopause, stable partner, education (>12 years), physical activities

Risks factors	*Odds ratio*	*95% confidence interval*
Arterial hypertension	4.29	3.47–5.31
Psychotropic drug use	1.54	1.22–1.94
Age ≥ 50 years	1.48	1.17–1.86
Body mass index ≥ 25 kg/m^2	1.47	1.15–1.89
Hormonal therapy	1.46	1.11–1.92
Waist circumference ≥ 88 cm	1.32	1.06–1.65
Alcohol consumption (≥ once/week)	0.73	0.54–0.98
Living in high cities (≥ 2500 m)	0.70	0.53–0.91
Living in hot cities (≥ 30°C)	0.67	0.51–0.88
Use of contraceptives	0.55	0.35–0.87

prevalent in diabetic women, considering that there is a substantial overlap between diabetes and hypertension in etiology and disease mechanisms. Obesity, inflammation, oxidative stress and insulin resistance are thought to be the common pathways[24].

Our study also found that aging is another factor that increases the risk of diabetes in women. When comparing women of 40–44 years of age with women of 55–59 years, the risk for the latter is tripled. This progression of risk is similar to the findings of the Italian study about diabetes during climacteric which indicates that, if we consider women < 50 years of age as the risk base, the OR of diabetes increases from 1.31 in women of 50–52 years of age to 1.66 in women of 53–56 years of age and to 2.84 in women > 56 years of age[25]. In the association of diabetes with age, the increase in the accumulation of abdominal fat that is produced with age plays a very important role. Moreover, the decline in the size and the strength of the muscles, which are important tissues for glucose metabolism, lead to the reduction of physical activity in older people. These changes finally lead to an increase of insulin resistance[26]. To this, it is necessary to add that several abnormalities in beta-cell islets and insulin secretion have also been pointed out in elderly people (i.e. increased amyloid deposition and decreased amylin secretion, impaired insulin secretion pulsatility, decreased insulin sensitivity of pancreatic beta-cells to insulinotropic gut hormones and diminished insulin response to non-glucose stimuli such as arginine)[25]. Therefore, there is an interplay between increased insulin resistance and decreased insulin secretion that largely explains the abnormal glucose metabolism seen in the elderly.

The factors BMI ≥ 25 kg/m^2 and abdominal perimeter ≥ 88 cm were also found as risk factors for diabetes in these women. Our results agree with most of the studies that assess some of these parameters as risk factors for diabetes. For example, one study[25] in women indicates an increase of risk for diabetes of 4.49 when women with BMI ≥ 26 kg/m^2 are compared with women with BMI < 24 kg/m^2. The relationship between being overweight and diabetes is a widely known and accepted concept, but this relationship seems to change in some ethnic groups. For instance, the risk of diabetes increases in Asian populations with a lower BMI than in Western populations[27].

Regarding the influence of menopause on the risk of diabetes, our study showed in the univariate analysis that postmenopausal women, natural or surgical, were more likely to have diabetes and this risk persisted when adjusting only for age. This result is consistent with the Italian study about menopause and diabetes that shows that women with natural menopause have a higher risk of diabetes in all age strata[25]. Nevertheless, when in our model of logistic regression we included risk variables other than age, natural or surgical postmenopause disappeared as a risk factor for diabetes. Similarly, an American study did not show any association between natural menopause and the risk for diabetes[28]. A recent study that analyzes this topic concluded that diabetes risk appears to be more strongly linked with factors associated with chronological aging and sex hormones rather than changes in menopausal status *per se*[7].

Different studies have shown that postmenopausal HT reduces the risk of diabetes mellitus[25,29–31]. Nevertheless, our study demonstrated that HT increases the risk for diabetes. However, this population is ethnically different from those studied in previous publications and may have genetic variants of estrogen receptors that could determine a different risk from that of Anglo populations, among which most of the studies have been carried out. In fact, polymorphisms of estrogen receptors α have been described in diabetic women that, when present, are associated with low levels of adiponectin[32],

Table 4 Women with natural menopause at different ages according to the absence or presence of type II diabetes

Age (years)	*Number of women*	*Number of postmenopausal women*	*% postmenopausal women (95% confidence interval)*		*Odds ratio (95% confidence interval)*
			Non-diabetic	*Diabetic*	
40–44	1082	150	13.2 (11.2–15.4)	29.5 (16.8–45.2)	2.76 (1.32–5.67)
45–49	1462	384	25.9 (23.6–28.3)	35.0 (23.1–48.4)	1.54 (0.86–2.75)
50–54	1464	901	61.7 (59.1–64.3)	59.3 (48.5–69.5)	0.91 (0.57–1.43)
55–59	1112	1112	100.0	100.0	–

Table 5 Climacteric symptomatology in diabetic and non-diabetic women

Domains	% prevalence of symptomatology (95% confidence interval)		Odds ratio (95% confidence interval)
	Non-diabetic	Diabetic	
Somatic domain			
Hot flushes, sweating	55.3 (54.0–56.6)	58.0 (53.1–62.8)	1.12 (0.91–1.38)
Heart discomfort	34.5 (33.3–35.7)	37.3 (32.7–42.2)	1.13 (0.91–1.40)
Sleep problems	61.5 (60.2–62.8)	70.7 (66.0–75.0)	1.51 (1.20–1.90)
Joint/muscular discomfort	66.3 (65.0–67.5)	73.7 (69.1–72.8)	1.42 (1.13–1.80)
Psychological domain			
Depressive mood	58.1 (56.8–59.3)	62.2 (57.3–66.9)	1.19 (0.96–1.47)
Irritability	59.0 (57.7–60.3)	60.5 (55.6–65.2)	1.06 (0.86–1.32)
Anxiety	47.4 (46.1–48.7)	54.1 (49.2–59.0)	1.31 (1.06–1.61)
Physical mental exhaustion	68.8 (67.6–70.0)	77.3 (72.9–81.2)	1.54 (1.21–1.98)
Genitourinary domain			
Sexual problems	44.6 (43.3–45.9)	51.0 (46.0–55.9)	1.29 (1.05–1.59)
Bladder problems	40.6 (39.3–41.9)	49.0 (44.1–54.0)	1.41 (1.14–1.73)
Dryness of vagina	46.9 (45.6–48.2)	57.3 (52.4–62.1)	1.52 (1.23–1.87)
Impaired quality of life (MRS score: ≥ 17)	13.9 (13.0–14.8)	17.8 (14.3–21.9)	1.34 (1.02–1.77)

Table 6 Goldberg Anxiety-Depression Scale in diabetic and non-diabetic women

	'Yes' answers (%)		
	Non-diabetic ($n = 5669$)	Diabetic ($n = 410$)	*p Value*
Depression items			
Have you been lacking in energy?	55.8	62.4	< 0.08
Have you lost interest in things?	30.7	38.0	< 0.001
Have you lost confidence in yourself?	18.5	20.3	ns
Have you felt hopeless?	21.7	23.9	ns
Have you had difficulty concentrating?	7.0	8.3	< 0.008
Have you lost weight (due to poor appetite)?	7.0	7.8	ns
Have you been waking early?	7.0	7.6	< 0.005
Have you felt slowed up?	39.2	48.0	< 0.0004
Have you tended to feel worse in the morning?	32.5	39.8	< 0.002
% Depression (≥ 3 'yes' answers)	45.9	55.1	< 0.002
Anxiety items			
Have you felt keyed up or on edge?	45.2	48.8	ns
Have you been worrying a lot?	58.2	60.2	ns
Have you been irritable?	40.4	42.2	ns
Have you had difficulty relaxing?	40.0	42.9	ns
Have you been sleeping poorly?	51.1	62.2	< 0.0001
Have you had headaches or neck aches?	60.5	67.6	< 0.004
Have you had any of the following: trembling, tingling, dizzy spells, sweating, diarrhea?	47.9	53.2	< 0.03
Have you been worrying about your health?	55.4	66.3	< 0.0001
Have you had difficulty falling asleep?	47.3	60.5	< 0.0001
% Anxiety (≥ 4 'yes' answers)	59.3	65.6	< 0.01

ns, not significant

a condition involving increased risk of diabetes[33]. A second possible explanation may be that the women in our study, unlike those of the previous studies, were evaluated several years after the publication of the Women's Health Initiative study which introduced changes in HRT prescription that include the use of lower doses of estrogen. Interestingly enough, women in our study who used oral hormonal contraceptives (which have more powerful metabolic effects than estrogen hormone therapy), had a lower risk of diabetes, the same as that of the pre-WHI women. Hormonal synthetic steroids that are present in oral contraception are related to the risk of deterioration in glucose tolerance because they induce insulin resistance.

The factors associated with lower risk of DM-II in our study, besides oral contraceptives, include living in high cities or in places with hot weather. The Pan American Health Organization, in agreement with our observation, has indicated that the prevalence of DM-II in populations located at >3000 m above sea level is almost half of what was found in similar socioeconomic and ethnic populations living in cities at lower levels[34].

The greater capture of glucose by the muscular tissue, caused by the chronic hypoxia, could be one of the causes of this lower risk of diabetes[35]. Conversely, our study found that living in cities with hot weather is an independent protective factor. Nevertheless, we have not been able to find in the literature a relationship between temperature and the risk of diabetes. Another protective factor is alcohol consumption. High alcohol consumption increases the risk of abnormal glucose regulation in men. In women, the associations are more complex, with a decreased risk with low or medium intake and increased risk with high alcohol intake[36].

This study demonstrated that the age of menopause in diabetic women was lower than in non-diabetic women (48.5 vs. 50.1 years of age). The Study of Women's Health Across the Nation (SWAN) in a multi-ethnic sample in the USA showed the same trend, but with a greater difference, 2.8 years less in the age of menopause in diabetic women[37]. However, that study included type I diabetic women, a group where menopause had occurred 6 years earlier than in the women of the control group[38]. In contrast, our study only included women with type II diabetes, which might explain the difference that exists with the SWAN results. Likewise, this last study includes mainly Caucasian and Afro-American women (95%), while our study only includes Hispanic women. Conversely, when carrying out a stratified analysis, we observed that the risk of diabetic women of becoming menopausal vs. non-diabetic women was almost tripled in women from 40 to 44 years of age, but in older women this difference disappeared. This observation may lead us to consider that there is a subgroup of diabetic women in whom the metabolic disorders of the disease will accelerate reproductive aging, and they will therefore experience an early menopause. Alternatively, other groups of diabetic woman would not follow this trend towards an earlier menopause, which will explain our observation that diabetic women >45 years of age have the same risk of experiencing menopause as non-diabetic women.

This study has the limitations of cross-sectional studies carried out with scales that may lead to subjective outcomes. The strength of this study is the involvement of a wide population of women from different countries of Latin America.

As a final point, in relation to the effect of diabetes on climacteric symptoms in the univariate analysis, we found deterioration in the quality of life due to this symptomatology in diabetic women. A pooled analysis of a population with DM-II in Germany, stratified by age and sex and using an instrument of life non-specific for climacteric (36-item Short Form Health Survey), also indicates that DM-II significantly deteriorates the quality of life of women, especially in regard to mental health[39]. Nevertheless, in our study, using a specific questionnaire to assess the quality of life in the climacteric (MRS) and after adjusting for related confounding factors, we found that the deterioration in the quality of life associated with the diabetes, as shown in the univariate analysis, would disappear.

CONCLUSION

This study indicates that the prevalence of type II diabetes reported (6.7%) is in agreement with the value projected for Latin America during this decade. Obesity, age, arterial hypertension and the use of psychotropic drugs are associated with a higher risk of diabetes. Menopause does not increase this risk. In contrast, diabetes triples the risk of menopause in women <45 years of age. Although diabetic women have a higher risk of experiencing climacteric symptoms and deterioration of their quality of life, this greater risk disappears if it is adjusted by variables such as age, obesity and hypertension, among others.

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Conflict of interest The authors report no conflict of interest. The authors alone are responsible for the content and writing of this paper.

Source of funding Nil.

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