



The comorbidity burden of type 2 diabetes mellitus (T2DM): sex differences and associated factors among 830 cases in North-Eastern Morocco

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Abstract

Background and aim Type 2 diabetes is prone to numerous comorbidities resulting from complex mechanisms involving hyperglycemia, insulin resistance, low-grade inflammation and accelerated atherogenesis. The purpose of the present study was to investigate these disorders and their associated risk factors according to patient sex in a population of type 2 diabetics in North-Eastern Morocco.

Methods This study was conducted in a medical analysis laboratory over a 1-year period from 01/10/2018 to 01/10/2019. This epidemiological study was carried out on 830 subjects aged 18 and over. Quantitative variables were expressed as means \pm standard deviation, and qualitative variables as frequencies and percentages. Hypothesis tests used to compare means and proportions were Student's *t*-test and Chi-square test of independence, respectively. Logistic regression was used to predict risk factors for each diabetes.

Results 830 patients were surveyed. 95.66% had diabetes-related comorbidities. Hypertension (23.7%), nephropathy (18.19%), dyslipidemia (14.82%), thyroid dysfunction (10.72%), cataract (10.12%), diabetic foot (7.23%), ketoacidosis (6.27%), retinopathy (3.49%), and skin disorders (2.77%) were observed. Sex was associated with dyslipidemia ($p=0.025$), hypertension ($p=0.032$) and retinopathy ($p=0.029$). Uncontrolled blood sugar, unbalanced lipid profile, age, physical activity, obesity, smoking, and alcohol consumption were risk factors with differential involvement in the occurrence of the mentioned pathologies.

Conclusions The results of our study showed that a significant proportion of the population suffers from diabetic comorbidities. To meet this challenge, further research is needed to identify the mechanisms of action of these factors, to control them and combat diabetogenic environments by setting up adapted educational programs.

Keywords Type 2 diabetes · Management · Glycemic control · Comorbidities · Educational programs · Sex

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Introduction

Globally, the number of people with diabetes has surged from 108 million in 1980 to 422 million in 2014, according to the World Health Organization. This increase has been most pronounced in low- and middle-income countries, and the Eastern Mediterranean region has been disproportionately impacted. In Morocco, diabetes affects 12.4% of adults, and causes over 12,000 deaths annually, with an additional 32,000 deaths attributable to complications of high blood sugar [1].

Multimorbidity, comorbidity, and diabetes complications are medical concepts that relate to different aspects of health and associated medical conditions. Multimorbidity refers to the presence of two or more chronic diseases (or medical conditions) in the same individual. These chronic diseases can be independent of each other and are not necessarily related to a primary disease. Comorbidity refers to the simultaneous presence of two or more diseases or medical conditions in the same individual. However, unlike multimorbidity, comorbidities are often related or associated in some way. For example, type 2 diabetes is frequently associated with obesity and high blood pressure due to common risk factors and similar underlying mechanisms. Diabetes complications are health problems that result from poorly controlled diabetes over time [2, 3].

Type 2 diabetes is managed through weight loss, a balanced diet, and regular physical activity. If these measures are not enough, antidiabetic drugs may be prescribed, starting with tablets and then injections if needed. Treatment aims to reduce the risk of complications by keeping blood sugar levels within the normal range [4]. Without proper management, diabetes can lead to life-threatening complications (nephropathy, neuropathy, retinopathy, coronary heart disease, myocardial infarction, peripheral arterial disease, and stroke), or alternatively, it increases the risk of comorbidities or even multimorbidities (hypertension, obesity, dyslipidemia, kidney disease, eye problems, skin disorders, thyroid dysfunction, ketoacidosis, diabetic foot), which can be expensive, debilitating, and can significantly reduce quality of life [5–7].

Sex largely influences the epidemiology, pathophysiology, clinical manifestations, disease progression, and response to treatment of type 2 diabetes (T2DM). Therefore, sex is an important determinant of health that should be considered when planning preventive-curative personalized medicine approaches. Globally, the prevalence of T2DM is increasing, particularly among women [8, 9].

Many health organizations are urging that a sex dimension be integrated into all phases of biomedical research, to improve both the quality and societal relevance of

scientific studies [10]. Multiple studies have shown that men with diabetes are more likely to develop microvascular complications (nephropathy, neuropathy, and retinopathy) than women. However, women with diabetes are at higher risk for macrovascular complications (coronary heart disease, myocardial infarction, peripheral arterial disease, and stroke), while the consequences of macrovascular complications may be greater for women [11–14]. Despite the sex disparities in the occurrence of diabetes-related disorders described earlier, the evidence is incomplete, and studies sometimes contradict each other [15, 16]. This study aims to investigate sex differences in diabetes-related comorbidities and sex-specific correlates of associated risk factors among type 2 diabetics in North-Eastern Morocco. We hypothesize that: (1) Diabetes-related complications/comorbidities differ between men and women. (2) Demographic (age and education), health (alcohol intake, smoking, exercise, depressive symptoms, body mass index, and hypertension), and diabetes (diabetes duration and HbA1c) risk factors are associated with diabetes.

Participants and methods

Study participants

This epidemiological study was conducted in Nador, Morocco, from October 1, 2018, to October 1, 2019, at a private medical laboratory. The study enrolled 830 men and women aged 18 or older. After obtaining approval from the Ministry of Health delegation in Nador to conduct the study in a medical analysis laboratory, we explained the study's purpose to the laboratory director, a medical biologist. Participants were type 2 diabetic patients who visited the laboratory to monitor their blood glucose levels, and whose blood glucose levels were ≥ 7 mmol/L on two occasions. With the help of a pre-trained team of two nurses and the medical biologist, we explained the study's purpose to the patients. Those who volunteered signed the consent form and completed a survey. We collected sociodemographic (age, marital status, education level, and employment status) and clinical information. Exclusion criteria were applied, and the following participants were excluded: pregnant or breastfeeding women, children, patients with type 1 diabetes, and patients with gestational diabetes. Appropriate precautions were taken in accordance with the Declaration of Helsinki [17].

Data collection and laboratory measurement

For each fasting participant (12 h of fasting), the laboratory nurse collected two vials of blood from a vein at the

elbow using a loose tourniquet and single-use needles. The blood was collected into vacuum-sealed tubes: one dry tube (lithium heparin-glass) for fasting blood glucose and one EDTA tube (ethylene-diamine-tetra-acetic acid) for glycated hemoglobin. Fasting blood glucose was measured 5 min after decantation and 10 min after centrifugation using an automated biochemistry machine. HbA1c was measured in whole blood using a high-performance liquid chromatography machine.

To assess participants' anthropometry, researchers measured their height, weight, and waist circumference (WC). Participants wore light clothing and removed their shoes while researchers measured their body weight and height to the nearest 0.1 kg and 0.1 cm, respectively. Body mass index (BMI) was calculated by dividing weight in kilograms by the square of height in meters. Researchers collected coexisting conditions according to patient's clinical history and past medical records (including systemic hypertension, cataract, dyslipidemia, diabetic foot, ketoacidosis, diabetic retinopathy, diabetic kidney disease, skin damage, thyroid dysfunction).

Operational definitions

Hypertension

We defined hypertension as blood pressure exceeding 140/90 mmHg, consistent with World Health Organization guidelines [18]. In our study, participants were classified as hypertensive if they reported a prior diagnosis, had a documented systolic blood pressure (SBP) \geq 140 mmHg or diastolic blood pressure (DBP) \geq 90 mmHg, or were taking prescribed antihypertensive medication.

Dyslipidemia

Dyslipidemia refers to abnormal levels of lipids in the blood, such as cholesterol and triglycerides. The main types include hypercholesterolemia (total cholesterol exceeding 2 g/L (5 mmol/L) or LDL cholesterol exceeding 1.60 g/L (4.1 mmol/L)), hypertriglyceridemia (triglycerides exceeding 1.50 g/L (1.7 mmol/L)), and low HDL cholesterol (below 0.40 g/L (1.7 mmol/L), often called "good cholesterol") [19]. In our study, we classified individuals as dyslipidemic if they met WHO criteria for at least one of these lipid disorders and had a documented diagnosis with medication prescribed for the condition.

Diabetic kidney disease

Diabetic nephropathy is a serious complication of diabetes that damages the kidneys over time due to high blood sugar [20, 21]. This damage prevents the kidneys from filtering

waste and fluids properly, leading to protein leakage and potential kidney failure. The study was based on the medical records of patients, all of whom had been confirmed by their treating physician to have diabetic nephropathy and all stages of diabetic nephropathy have been considered.

Thyroid dysfunction

Refers to any problem that affects the normal functioning of the thyroid gland. This can include excessive or insufficient production of thyroid hormones, which can lead to various symptoms and health issues [22]. A patient with thyroid dysfunction is defined by an abnormal TSH level (normal TSH range is between 0.4 and 4.5 mIU/L) or by taking a thyroid medication.

Cataract

Cataracts are the opacification of the crystalline lens inside the eye, causing a reduction in near and distance vision that cannot be improved by optical correction. The only treatment is surgery. Patients who have undergone cataract surgery after being diagnosed with diabetes have been confirmed as cases.

Diabetic retinopathy

Diabetic retinopathy is a serious complication of diabetes characterized by damage to the blood vessels of the retina, which can lead to vision loss. Symptoms may include blurred vision, dark spots or difficulty seeing at night [23, 24]. Our study was based on patients with confirmed diabetic retinopathy followed regularly by an ophthalmologist.

Skin damage

Up to half of diabetic patients experience skin problems. These can be broadly categorized into three groups: those specific to diabetes (e.g., lipoid necrobiosis), complications arising from the disease itself (like fungal infections), and issues related to diabetes medications [25]. Positive cases for skin lesions focused on patients who reported having skin problems or having consulted a dermatologist about them.

Diabetic ketoacidosis

A serious complication of diabetes characterized by hyperglycemia, hyperketonemia, and metabolic acidosis [26]. It is less common in type 2 diabetes, but may appear in case of infection, physical or emotional stress, poor diabetes management, or lack of insulin. All diabetic patients with a history of hospitalization for this complication were included.

Obesity

A person is considered obese if his or her BMI exceeds 25 kg/m², so we have merged overweight and obesity.

Regular physical activity

A person was regularly physically active if he or she exercised at least twice a week at a physical activity that increased heart and breathing rates.

Controlled blood glucose

A person was in regular control of his/her blood glucose if he/she measures his/her blood glucose themselves or in a dedicated health center at least twice a month.

Statistical analysis

SPSS version 26 and WHO Anthroplus version 1.04 software were used to analyze the data. Continuous variables were presented as means and standard deviations, while categorical variables were summarized as frequencies and percentages. The independent Student's *t*-test was used for continuous variables and Chi-square tests were used to assess significant differences between categorical variables. Multivariate backward regression model was used to determine significant risk factors associated with hypertension. We report crude odds ratios (COR), adjusted odds ratios (AOR), and their respective 95% confidence intervals (CI) as the measure of association.

Results

Characteristics of participants

Researchers recruited 830 participants for the study, consisting of 27.2% men and 72.8% women. The average age of the participants was 59.06 ± 14.51 years, with the age group 55–70 years being the most prevalent at 44%. In terms of educational level, 64.94% were illiterate, with 62.8% of them being women. Among the participants, 90.2% were unemployed, with 68% of them being women. Additionally, 86.4% of the sample were married. Regarding anthropometric measurements, the mean weight for men was 81.25 ± 13.68 kg, while for women, it was 79.8 ± 15.45 kg. The average height for women was 162.85 ± 11.05 cm, and for men, it was 167.7 ± 10.67 cm. Body mass index calculations revealed a prevalence of obesity among type 2 diabetics at 47.9%, with 36.9% of them being women. Underweight was estimated at 5.4%, with a predominance of women at 2.4%. Concerning diabetes characteristics, the population

had a mean fasting blood glucose of 2.32 ± 0.78 g/L, with a minimum blood glucose of 0.46 g/L and a maximum blood glucose of 5.55 g/L. The mean blood glucose level was 2.25 ± 0.708 g/L in men and 2.34 ± 0.81 g/L in women. The mean glycosylated hemoglobin was 9.43 ± 2.14 in women and 9.25 ± 2.38 in men. The duration of diabetes was 7.51 ± 3.95 years for women and 7.55 ± 4.07 years for men. Concerning self-medication habits, 4.45% of women used traditional self-medication, while only 1.08% of men used traditional medicines to treat diabetes. In terms of toxic habits, 7.7% of diabetics were smokers, including 6.86% of men and 0.81% of women. Additionally, 2.28% were regular alcohol consumers, with 1.92% being men and 0.36% being women. The results are summarized in Table 1.

Association between diabetes comorbidities and patient sex

The study revealed that only 4.34% (*n* = 36) of patients had no comorbidities related to diabetes. Hypertension was the most prevalent, affecting 23.37% of patients (*n* = 194), including 153 women and 41 men. Diabetic nephropathy had a prevalence of 18.19% (*n* = 151), with 107 cases in women and 44 in men. Dyslipidemia was present in 14.82% of the sample (*n* = 118), with 76 cases in women and 42 in men. Thyroid dysfunction affected 10.72% (*n* = 89) of patients, including 68 women and 21 men. Cataracts were diagnosed in 10.12% (*n* = 84) of the patients, with 59 women and 25 men affected. Diabetic foot was found in 7.23% (*n* = 60) of the cases, including 45 women and 15 men. Ketoacidosis was present in 6.27% (*n* = 52) of patients, with 39 women and 13 men affected. Diabetic retinopathy concerned 3.49% (*n* = 29) of the patients, including 18 women and 11 men. Skin involvement was diagnosed in 2.77% (*n* = 23), including 16 women and 7 men.

The Chi-square test revealed a significant association between patient sex and three diseases: dyslipidemia (*p* = 0.025), arterial hypertension (*p* = 0.032), and diabetic retinopathy (*p* = 0.029) Table 2.

Factors associated with diabetes comorbidities by sex

A multivariate logistic regression analysis was conducted to identify predictors of pathologies previously linked to sex. To enhance the results of the logistic regression, categorical variables were converted into dummy variables (dichotomized). Outliers were examined and it was determined that all residual values were randomly distributed within the range of − 3 to 3 z-scores.

The exploration of risk factors associated with diabetic multimorbidity revealed several findings. Table 3 illustrates the risk factors associated with dyslipidemia. The

Table 1 Sample characteristics

	Women		Men		Sig. (X^2 or t)
	F	n	F	n	
Age range (Years)					
[18–25]	1.8	15	0.7	6	0.012
[25–40]	4.9	41	3.7	31	
[40–55]	18.1	150	6	50	
[55–70]	33.6	279	10.4	86	
> 70	14.5	120	6.3	52	
Education					
Illiterate	62.8	521	2.14	178	0.002
Primary	3.5	29	0.7	6	
Secondary	2.4	20	1.9	16	
Higher	4.2	35	3	25	
Occupation					
No	68	564	22.2	184	<0.001
Yes	4.9	41	4.9	41	
Marital status					
Single	3	25	1.4	12	0.006
Divorced	1.4	12	1.3	11	
Married	64.7	537	21.7	180	
Widowed	3.7	31	2.7	22	
Blood glucose (g/l)	2.34 ± 0.81		2.25 ± 0.708		0.618
HbA1c (%)	9.43 ± 2.14		9.25 ± 2.38		0.41
TC	1.991 ± 0.46		1.992 ± 0.44		0.289
HDL-C	0.52 ± 0.13		0.53 ± 0.14		0.582
LDL-C	0.88 ± 0.27		0.91 ± 0.30		0.048
TG	1.32 ± 0.79		1.27 ± 0.55		0.067
Diabetes duration (Years)	7.51 ± 3.95		7.55 ± 4.07		0.76
Height (cm)	162.85 ± 11.056		167.71 ± 10.671		0.001
Weight (Kg)	79.80 ± 15.45		81.25 ± 13.68		0.214
Self-medication					
Yes	4.45	37	1.08	9	0.236
No	68.43	568	26.02	216	
BMI Kg/m ²					
Underweight	2.4	20	0.4	3	0.014
Normal weight	14.4	119	7.5	62	
Overweight	19.1	157	8.3	68	
Obesity	36.9	307	11	94	
Toxic habits					
Smoking	0.84	7	6.86	57	<0.001
Alcohol use	0.36	3	1.92	16	

HbA1c glycated hemoglobin, F Frequency, n effectif, X^2 Chi-Square, t Student test, BMI Body Mass Index

probability of dyslipidemia increased with advancing age for both sexes. Men above 71 years were approximately three times AOR = 2.8, (95% CI, 1.1–3.2) more at risk of dyslipidemia compared to participants aged 18–25 years, for women the risk is less pronounced AOR = 2.09, (95% CI, 1.55–4.59). The study found that both single and divorced men were more likely to have dyslipidemia compared to married men. Specifically, single men had a roughly two-fold greater risk (2.06 times higher), while divorced men had a 1.5-fold increased risk. Interestingly, marital status was not a risk factor for dyslipidemia in women. High levels

of total cholesterol were positively associated with dyslipidemia, the odds ratio in males was AOR = 1.85, (95% CI: 0.24–3.82) and in females AOR = 1.28, (95% CI: 0.44–6.7). The adjusted odds ratio showed that people with high LDL-C level were 1.59 times for men AOR = 1.28, (95% CI: 0.44–6.7) and 1.75 times for women AOR = 1.28, (95% CI: 0.44–6.7) more likely to suffer a dyslipidemia than those who had a normal LDL-C level. However, the high level of triglyceride and low level of HDL-C showed no association with dyslipidemia. Body mass index above 25 kg/m² was associated with dyslipidemia for both sexes. Being

Table 2 Association between diabetes comorbidities and patient sex

Complications	Sex		Chi square test p-value
	Women	Men	
Dyslipidemia	76	42	0.025*
Yes	529	183	
No			
Diabetic foot	45	15	0.703
Yes	560	210	
No			
Hypertension	153	41	0.032*
Yes	452	184	
No			
Ketoacidosis	39	13	0.724
Yes	566	212	
No			
Diabetic retinopathy	18	11	0.029*
Yes	547	214	
No			
Cataract	59	25	0.564
Yes	546	200	
No			
Diabetic kidney disease	107	44	0.535
Yes	498	181	
No			
Skin damage	16	7	0.716
Yes	589	218	
No			
Thyroid dysfunction	68	21	0.430
Yes	537	204	
No			

df degree of freedom

overweight or obese increased the odds of dyslipidemia by AOR = 1.96, (95% CI: 0.8–6.18) for men and AOR = 1.97, (95% CI: 0.86–4.51) in women compared to having normal BMI. Regular physical activity appears to be a protecting factor against dyslipidemia in both men AOR = 0.41, (95% CI: 0.06–1.2) and women AOR = 0.68, (95% CI: 0.56–1.83). In the adjusted model, current alcohol consumption was significantly associated with dyslipidemia for men only. Indeed, regular drinkers were approximately two times AOR = 1.96, (95% CI, 0.78–5.26) more at risk of dyslipidemia compared to non-alcohol drinkers.

Increasing age is associated with a significantly higher likelihood of developing hypertension. Compared to young adults (aged 18–25), the odds of hypertension were nearly doubled (AOR = 1.91, 95% CI: 0.23–3.50) for those aged 56–70. This risk further increased for individuals aged 71 and above, who were four times more likely to develop hypertension (AOR = 8.23, 95% CI: 4.09–16.55). Similar trends were observed in women, with a slight increase in risk compared to men. Women aged 56–70 had an odds ratio of 2.50 (95% CI: 1.02–4.10), while those aged 71 and above had an even higher risk (AOR = 4.50, 95% CI:

2.50–6.30). Having high total cholesterol levels was associated with an increased likelihood of hypertension in both men and women. Compared to those with normal cholesterol, men with high cholesterol had an odds ratio of 1.21 (95% CI: 0.85–1.73) for hypertension. Similarly, women with high cholesterol had an odds ratio of 1.13 (95% CI: 0.63–1.91). Men with high triglycerides had a one-and-a-half times greater risk of hypertension (AOR = 1.59, 95% CI: 1.15–2.58) compared to men with normal triglyceride levels. Similarly, women with high triglycerides were also at increased risk, with an odds ratio of 1.36 (95% CI: 0.74–2.01) compared to their counterparts. Obese men were found to have a three-fold increased risk of hypertension (AOR = 3.18, 95% CI: 0.83–6.91) compared to non-obese men. Similarly, obese women exhibited a nearly three-fold greater likelihood of hypertension (AOR = 2.61, 95% CI: 1.3–4.4) compared to their non-obese counterparts. Regular blood glucose control was associated with a significant reduction in hypertension risk. Men with regular blood glucose control had a 61% lower risk (AOR = 0.27, 95% CI: 0.08–1.35) compared to those without regular control. Similarly, women with regular blood glucose control experienced a 67% reduction in risk (AOR = 0.33, 95% CI: 0.14–1.11). Regular physical activity was associated with a significant reduction in hypertension risk. Engaging in physical activity lowered the odds of hypertension by 56% (AOR = 0.27, 95% CI: 0.06–1.46) for men. Similarly, women who regularly participated in sports experienced a 68% reduction in hypertension risk (AOR = 0.32, 95% CI: 0.18–1.43). Alcohol consumption and smoking were found to be significant risk factors for dyslipidemia, but only among men. Men who were both regular drinkers and regular smokers had roughly double the risk of dyslipidemia (AOR = 2.04, 95% CI: 1.7–5.02) and (AOR = 1.89, 95% CI: 0.78–5.26) respectively, compared to those who did not drink or smoke regularly. Table 4.

Table 5 presents the association between various risk factors and diabetic retinopathy, analyzed using multiple logistic regression. When controlling for other variables, high total cholesterol emerged as a significant risk factor for both men and women. Men with high total cholesterol had an odds ratio (AOR) of 2.0 (95% CI: 1.46–2.65) for developing diabetic retinopathy, while the AOR for women was 1.6 (95% CI: 1.12–2.15). Another factor is obesity. Men with obesity have an adjusted odds ratio (AOR) of 3.07 (95% CI: 0.72–9.93) for developing diabetic retinopathy, while women with obesity have an AOR of 2.50 (95% CI: 0.26–5.33). Uncontrolled blood sugar is a further risk factor for diabetic retinopathy. Men with uncontrolled blood sugar had an AOR of 0.69 (95% CI: 0.37–2.24), while women with uncontrolled blood sugar had an even higher AOR of 0.22 (95% CI: 0.03–1.07). Sedentary behavior also increases the risk of diabetic retinopathy. Men with sedentary lifestyles have an

Table 3 The unadjusted and adjusted odds ratio of the association between risk factors and dyslipidemia in participants by sex

Risk factors	Dyslipidemia							
	Men				Women			
	COR	95% CI	AOR	95% CI	COR	95% CI	AOR	95% CI
Age groups (years)								
18–25	-ref		-ref		-ref		-ref	
26–40	0.1	0.01–0.63	0.95	0.24–3.82	0.19	0.1–2.38	1.28	0.44–3.7
41–55	0.120	0.09–0.3	1.79	0.58–5.51	0.36	0.24–1.64	2.31	0.94–5.69
56–70	0.31	0.04–1.7	3.9	1.74–6.84	0.52	0.36–2.75	1.96	1.23–3.15
≥ 71	3.7*	3.14–8.5	2.81*	1.1–3.2	3.63*	3.26–7.85	2.09*	1.55–4.59
Marital status								
Married	-ref		-ref		-ref		-ref	
Divorced	1.95*	0.03–3.2	1.5*	0.24–3.82	1.29	0.09–2.87	1.18	0.44–3.7
Single	2.2*	0.9–6.4	2.06*	0.58–5.51	0.26	0.14–1.36	0.31	0.14–5.69
Widowed	3.59	0.4–8.7	3.9	1.74–6.84	0.52	0.36–.85	0.96	0.23–7.15
High TC (TC ≥ 2g/L)								
No	-ref		-ref		-ref		-ref	
Yes	1.43*	0.71–2.87	1.85*	0.24–3.82	1.93*	0.09–3.38	1.28*	0.44–6.7
High TG (TG ≥ 1.5g/L)								
No	-ref		-ref		-ref		-ref	
Yes	0.8	0.37–1.76	0.95	0.24–3.22	0.79	0.06–0.52	0.28	0.14–0.9
High LDL-C (LDL-C ≥ 1.6g/L)								
No	-ref		-ref		-ref		-ref	
Yes	2.86*	0.09–7.63	1.59*	0.24–3.82	2.12*	0.09–3.38	1.75*	0.44–3.7
Low HDL-C (HDL-C < 0.4g/L)								
No	-ref		-ref		-ref		-ref	
Yes	0.98	0.39–2.41	0.96	0.78–1.85	1.49	1.22–2.26	0.31	0.97–1.51
Obesity (BMI ≥ 25kg/ m²)								
No	-ref		-ref		-ref		-ref	
Yes	3.67*	0.75–5.72	1.96*	0.8–6.18	2.08*	1.22–7.82	1.97*	0.86–4.51
Regular controlled blood glucose								
No	-ref		-ref		-ref		-ref	
Yes	0.3	0.1–1.7	0.66	0.08–1.42	1.66	0.4–2.82	0.21	0.97–2.11
Diabetes duration								
< 5 years	-ref		-ref		-ref		-ref	
≥ 5 years	0.89	0.02–1.2	0.71	0.3–1.67	0.72	0.53–.98	0.5	0.4–0.7
Regular physical activity practice								
No	-ref		-ref		-ref		-ref	
Yes	0.34*	0.12–1.5	0.41*	0.06–1.2	0.72*	0.14–1.14	0.68*	0.56–1.83
Toxic habits								
No	-ref		-ref		-ref		-ref	
Smoking	1.41	0.7–1.68	2.96	1.34–4.18	1.01	0.81–1.25	0.66	0.4–0.97
Alcohol use	2.88*	1.1–2.6	1.96*	0.78–5.26	2.57	2.02–.28	1.59	1.23–2.05

COR Crude odds ratio, AOR Adjusted Odds ratio, CI Confidence interval, ref Reference group, TC Total cholesterol, TG Triglyceride, LDL-c Low density lipoprotein cholesterol, HDL-c High density lipoprotein cholesterol

AOR of 0.61 (95% CI: 0.25–0.95), and women with sedentary lifestyles have an AOR of 0.55 (95% CI: 0.22–1.92). A risk factor that concerns men only is alcohol consumption, as alcoholics are twice 1.95 (95% CI: 0.67–4.25) as likely to develop diabetic retinopathy.

Discussion

The present study was conducted in patients with non-insulin-dependent type 2 diabetes. A total of 830 patients were enrolled, comprising 27.2% men and 72.8% women.

Table 4 The unadjusted and adjusted odds ratio of the association between risk factors and hypertension in participants by sex

Risk factors	Hypertension							
	Men				Women			
	COR	95% CI	AOR	95% CI	COR	95% CI	AOR	95% CI
Age groups (years)								
18–25	-ref		-ref		-ref		-ref	
26–40	0.68	0.46–1.03	0.49	0.18–2.56	1.10	1.1–3.36	1.36	1.07–3.4
41–55	1.46	0.68–3.12	1.23	0.41–3.70	1.36	1.34–1.64	3.31	1.04–5.60
56–70	2.01*	0.66–6.11	1.91*	0.23–3.50	2.30*	1.21–4.01	2.50*	1.02–4.10
≥71	4.34*	1.58–11.9	3.83*	1.82–8.05	4.40*	2.44–5.71	4.50*	2.50–6.30
Marital status								
Married	-ref		-ref		-ref		-ref	
Divorced	1.42	0.85–2.72	1.11	0.68–2.54	1.30	1.10–3.64	1.16	1.44–3.4
Single	1.26	0.7–1.97	1.27	0.53–2.15	1.36	1.34–1.36	1.31	1.14–5.60
Widowed	1.34	1.08–1.94	1.15	0.80–1.54	1.53	1.36–65	1.06	1.33–4.15
High TC (TC ≥ 2g/L)								
No	-ref		-ref		-ref		-ref	
Yes	1.53*	1.1–2.05	1.21*	0.85–1.73	1.62*	0.74–1.65	1.13*	0.63–1.91
High TG (TG ≥ 1.5g/L)								
No	-ref		-ref		-ref		-ref	
Yes	1.86*	1.18–2.73	1.59*	1.15–2.58	1.77*	1.15–3.10	1.36*	0.74–2.01
High LDL-C (LDL-C ≥ 1.6g/L)								
No	-ref		-ref		-ref		-ref	
Yes	1.44	1.23–1.95	1.49	0.88–2.45	3.13	1.10–3.36	1.45	1.44–3.4
Low HDL-C (HDL-C < 0.4g/L)								
No	-ref		-ref		-ref		-ref	
Yes	0.66	0.22–2.41	0.44	0.76–2.15	1.40	1.33–3.36	1.31	1.04–1.51
Obesity (BMI ≥ 25kg/ m ²)								
No	-ref		-ref		-ref		-ref	
Yes	4.67*	1.09–10.34	3.18*	0.83–6.91	2.33*	1.25–4.51	2.61*	1.3–4.4
Regular controlled blood glucose								
No	-ref		-ref		-ref		-ref	
Yes	0.54*	0.4–1.98	0.39*	0.08–1.35	0.61*	1.4–1.63	0.33*	0.14–1.11
Diabetes duration								
<5 years	-ref		-ref		-ref		-ref	
≥5 years	0.36	0.9–1.84	0.16	0.82–1.76	1.43	1.53–.06	1.5	1.4–1.4
Regular physical activity practice								
No	-ref		-ref		-ref		-ref	
Yes	0.41*	0.2–1.93	0.44*	0.06–1.46	0.31*	0.25–1.51	0.32*	0.18–1.43
Toxic habits								
No	-ref		-ref		-ref		-ref	
Smoking	3.22*	1.2–6.43	2.04*	1.7–5.02	1.11	1.06–1.35	1.66	1.4–2.84
Alcohol use	1.95*	0.46–3.23	1.89*	0.78–5.26	1.76	3.13–8.02	1.51	1.18–3.36

COR Crude odds ratio, AOR Adjusted Odds ratio, CI Confidence interval, -ref Reference group, TC Total cholesterol, TG Triglyceride, LDL-c Low density lipoprotein cholesterol, HDL-c High density lipoprotein cholesterol

The predominance of women in our study (72.8% of the cases) can be attributed to the higher utilization of health-care services by women with diabetes in comparison to men. This, in turn, reflects their tendency to monitor and manage their blood glucose levels more consistently [27]. Another

study by El Alami et al. revealed a high prevalence of type 2 diabetes among Moroccan women highlighting specific risk factors that contribute to this high prevalence. These include obesity, a sedentary lifestyle, and socio-economic factors such as low levels of education and precarious

Table 5 The unadjusted and adjusted odds ratio of the association between risk factors and DR in participants by sex

Risk factors	Diabetic retinopathy							
	Men				Women			
	COR	95% CI	AOR	95% CI	COR	95% CI	AOR	95% CI
Age groups (years)								
18–25	-ref		-ref		-ref		-ref	
26–40	0.57	0.35–1.02	0.39	0.07–2.45	0.53	0.2–2.25	0.25	0.06–2.3
41–55	0.35	0.07–2.02	0.82	0.33–2.62	0.29	0.13–1.53	2.20	0.03–4.50
56–70	2.09	0.55–5.21	0.91	0.22–2.49	2.23	0.20–3.05	1.40	0.02–3.06
≥71	3.23	1.47–8.54	2.72	0.72–7.04	3.30	2.33–4.61	3.40	2.40–5.29
Marital status								
Married	-ref		-ref		-ref		-ref	
Divorced	0.32	0.14–2.62	0.16	0.07–2.43	0.21	0.13–2.53	0.9	0.63–1.21
Single	0.95	0.6–2.96	0.26	0.12–2.04	0.25	0.23–2.25	0.7	0.47–0.93
Widowed	0.27	0.07–0.93	0.34	0.17–0.43	0.42	0.25–1.54	0.44	0.22–1.04
High TC (TC ≥ 2g/L)								
No	-ref		-ref		-ref		-ref	
Yes	1.7*	1.29–2.21	2*	1.46–2.65	1.5*	1.12–2.07	1.6*	1.12–2.15
High TG (TG ≥ 1.5g/L)								
No	-ref		-ref		-ref		-ref	
Yes	0.75	0.07–2.62	0.49	0.04–1.47	0.61	0.04–2.08	0.25	0.63–1.73
High LDL-C (LDL-C ≥ 1.6g/L)								
No	-ref		-ref		-ref		-ref	
Yes	1.4	0.93–2.06	1.2	0.69–2.12	1.5	1.02–2.48	1.6	1.02–2.47
Low HDL-C (HDL-C < 0.4g/L)								
No	-ref		-ref		-ref		-ref	
Yes	0.55	0.22–2.30	0.33	0.65–2.04	0.30	0.22–2.25	0.20	0.03–0.41
Obesity (BMI ≥ 25kg/ m2)								
No	-ref		-ref		-ref		-ref	
Yes	4.56*	0.9–11.23	3.07*	0.72–9.93	4.22*	1.24–7.40	2.50*	0.26–5.33
Regular controlled blood glucose								
No	-ref		-ref		-ref		-ref	
Yes	0.43*	0.3–0.97	0.69*	0.37–2.24	0.50*	0.3–0.52	0.22*	0.03–1.07
Diabetes duration								
<5 years	-ref		-ref		-ref		-ref	
≥5 years	4.9	3.6–6.8	4.5	3.16–6.48	2.5	1.9–3.19	2.13	1.78–3.06
Regular physical activity practice								
No	-ref		-ref		-ref		-ref	
Yes	0.28*	0.2–0.92	0.61*	0.25–0.95	0.25*	0.14–0.49	0.55*	0.22–1.92
Toxic habits								
No	-ref		-ref		-ref		-ref	
Smoking	4.5	1.48–8.72	3.4	1.71–8.44	1.3	0.83–2.18	1.4	0.81–2.25
Alcohol use	1.94*	0.35–2.22	1.95*	0.67–4.25	3.65	2.02–7.02	2.40	0.07–5.23

COR Crude odds ratio, AOR Adjusted Odds ratio, CI Confidence interval, -ref Reference group, TC Total cholesterol, TG Triglyceride, LDL-c Low density lipoprotein cholesterol, HDL-c High density lipoprotein cholesterol

socio-economic status [28]. A staggering 64.94% of the study participants were illiterate, with women disproportionately affected (nearly 63% of illiterate participants were women). This lack of education translated into high unemployment, with 90.2% of participants jobless. Women

again faced greater challenges, making up almost 68% of the unemployed. This difference can be explained by several factors, including unequal access to education and the persistence of cultural traditions that favor the education of boys [29]. Almost all patients included in the study (96.38%) had

T2DM-related multimorbidities. This value considerably exceeds those found internationally. Indeed, among 11,357 people with T2DM from 33 countries followed for three years, Arnold and her team reported in their study that 31.5% of patients had at least one microvascular complication, and 16.6% at least one macrovascular complication [30]. Furthermore, hypertension is the most prevalent comorbidity of T2DM in our population, with a rate of 23.37%. Our results concerning the prevalence of arterial hypertension remain lower than those found regionally and internationally. Oulad Sayad and colleagues reported a prevalence of 45% in Central Morocco [31], in Saudi Arabia Ziyad et al. reported a prevalence of 71.68% [32], in Jordan 75% [33], in the United States 75.4% [34]. The authors of many of these studies stated that blood pressure was not controlled, and the discovery of hypertension was fortuitous. Diabetic kidney disease in our population was estimated at 18.19%, which is lower than the worldwide prevalences of 38.8% in China [35], 34.4% in India [36], 45.7% in Egypt [37], in the USA, prevalence varies from 30 to 40% [38]. Dyslipidemia affects 14.8% of patients. This prevalence of dyslipidemia remains well below international rates, ranging from 81.5% in Ethiopia [39] to 88.9% in Thailand [40]. 10.72% of our patients had thyroid dysfunction, which is similar to studies in the literature [41, 42]. Compared with cataracts, diabetic retinopathy has a low prevalence, at 10.12% and 3.49% respectively. These rates remain relatively similar to the results found on an international scale, for cataracts a study including 42,469 diabetic adults from six countries (China, Ghana, India, Mexico, Russia, South Africa) has reported rates between 1.7% and 13.3% [43]. For diabetic retinopathy, the Global Burden of Disease Study on diabetic retinopathy in 2010 reported a worldwide prevalence of 34% [44], and 27.6% was reported in Japan [45]. It has been reported in the literature that ketoacidosis occurs in 1–29% of cases in type 2 diabetics. Our study is no exception to the general rule, with a prevalence of 6.27% [46, 47]. Diabetic foot ulcers (DFUs) are a common complication of diabetes that develops over time, especially when diabetes is not well controlled. Approximately one in five to three in ten people with diabetes worldwide will develop a DFU at some point in their lives [48, 49]. Concerning diabetic dermopathy, it is observed in 0.2 to 55% of diabetic patients [50]. In our population, the prevalence was estimated at 2.77%, which remains low, and this could be explained by the darker skin color of the residents of the study area, located in Eastern Morocco, which makes dermopathies difficult to discover and to seek treatment from a specialist.

Disparities in prevalences between countries could be explained by inequalities in socioeconomic status (education, income, employment), access to healthcare services (access, affordability, quality), environmental variables (exposure to a toxic environment, diabetogenic environment)

[51], or even by the methodology used to identify pathologies. Indeed, some authors use patient medical records or admission records for surgical procedures, while others rely on patient self-reporting.

The Chi-square test revealed a significant difference in the prevalence of dyslipidemia between diabetic men and women ($p=0.025$). This finding is confirmed by other studies. In fact, the prevalence of dyslipidemia was higher in women than in men [52, 53]. Investigations in Korea [54], and India [55] have also reported gender differences trends. Mechanisms underlying this gender related trend of prevalence in dyslipidemia between genders are not completely clear. Possible explanations for this trend of increase in females include menopausal transition and loss of estrogen, which might act as a trigger factor and enhance metabolic dysfunction [56, 57]. The factors identified as being significantly associated with dyslipidemia in multivariate logistic regression were older age in both sexes. This result is in line with previous studies. The possible reason, according to these authors, could be age-related degenerative effects. However, the exact mechanism has yet to be elucidated [58–60]. Our study also revealed a significant association between marital status and dyslipidemia. However, there is no clear explanation for single men being more likely to have dyslipidemia than married men. Although this may be due to the higher prevalence of unhealthy eating habits (excessive consumption of fat and fast food) that accompany divorce, separation, and widowhood, and which are more common in men than in women [61]. Multivariate analysis reported a significant association between LDL-C and dyslipidemia. Moreover, the t-test revealed a statistically significant difference between LDL-C levels in men and women and given that dyslipidemia is defined by the four components of the lipid profile, including LDL-C. This factor is thought to be involved in the difference in the prevalence of the complication between men and women [62]. In our study, obese men and women seem to be at the same level of risk of developing dyslipidemia, twice as much as normal weight subjects. Obesity is a major risk factor for dyslipidemia, a condition characterized by abnormal levels of fats (lipids) in the blood. Around 60–70% of obese individuals are estimated to have dyslipidemia and there are several ways obesity can contribute to dyslipidemia: increased production of triglycerides and LDL by the liver, Decreased HDL cholesterol levels or even Insulin resistance [63]. Regular physical activity appears to be a protecting factor against dyslipidemia in both men and women. Epidemiological studies provide clear evidence that physical activity can reduce cardiovascular morbidity and mortality by improving lipid profiles [64].

We also found a significant difference in the occurrence of hypertension between the two sexes ($p=0.032$). We therefore agree with the earlier findings of Azra et al. in Iran, who reported a higher risk of hypertension in men than in

women [65], and those of European clinicians indicating a high risk of hypertension and associated cardiovascular disease in males [66]. The odds of hypertension were nearly doubled for those aged 56–70. This risk further increased for individuals aged 71 and above, who were four times more likely to develop hypertension. Similar trends were observed in women, with a slight increase in risk compared to men. Several studies have attempted to explain this finding. Indeed, after menopause, the risk of hypertension in women increases, rapidly reaching that of men and even surpassing it from the seventh decade of life. The mechanisms by which estrogen deficiency increases the risk of hypertension have been extensively studied. These mechanisms are clearly multifaceted. However, it has not been clearly demonstrated that menopausal hormone treatment reduces blood pressure levels. The factors that cause hypertension to become more prevalent after the seventh decade in women are also certainly of multifactorial origin, notably a lower level of cardiovascular risk in women than in men, all other things being equal, with a higher life expectancy and a survivor effect [67]. Tobacco consumption was associated with hypertension. Several studies have reported tobacco as a risk factor associated with high blood pressure [68, 69]. Tobacco includes nicotine, which causes vasoconstriction of blood vessels [25]. It also activates the sympathetic nervous system, producing an increase in heart rate and blood pressure [70]. While other studies have found a significant association between smoking in women and hypertension [71], our study found no significant association between smoking and the onset of hypertension. Patients with a higher BMI were much more likely to develop hypertension than those with a normal BMI. This result is in line with several previous studies [28, 72, 73]. Research on laboratory animals and humans suggests that altered renal natriuresis due to physical compression of the kidneys by fat in and around them plays an important role in increasing blood pressure [74]. Patients (of both sexes) with high HbA1c levels—the other side of poorly controlled blood sugar levels—are more likely to suffer from hypertension. This result is in line with the findings of numerous other studies [75, 76]. This relationship is attributable to excess glucose in the blood, which traps lipoproteins, leading to atheroma formation and increased blood pressure [77]. Alcohol is also a risk factor for arterial hypertension, which increases blood levels of angiotensin II, known as a powerful vasoconstrictor [78]. The reason why women are exempt from this action could be explained by light or intermittent alcohol consumption, which would have no or even beneficial effects on blood pressure [79].

A significant difference was also observed in the occurrence of diabetic retinopathy (DR). This result is consistent with a study including 12,766 in China and reporting a high risk of DR in women. The mechanisms by which the female sex contributes to the prevalence of DR in T2DM patients

are still unknown [80]. An abnormally balanced lipid profile is a risk factor for the development of diabetic retinopathy. Our study revealed a significant association between high total cholesterol levels and diabetic retinopathy. Our results concur with those of Rema et al. which demonstrated that average cholesterol, triglyceride and non-HDL levels were higher in patients with DR than in those without [81]. Obesity has been shown to be a risk factor for DR, in line with the meta-analysis by Zhu et al. who, by analyzing 13 prospective cohort studies on obesity and DR risk, demonstrated the existence of a significant adverse effect on the incidence of DR [82]. Uncontrolled blood sugar is another risk factor for diabetic retinopathy in both sexes. These findings are in line with the findings of Hammoudi and his team [83]. However, regular physical activity in men appears to play a protective role against diabetic retinopathy. Ren and his team examined data from 22 studies and showed that physical activity was found to have a protective association with DR via its hypoglycemic action [84]. Evidence for the involvement of alcohol in the incidence of DR is contradictory. Our study revealed a significant association between alcohol consumption and diabetic retinopathy only in men. This association was explained by the negative action of alcohol on the inflammatory response and oxidative stress could be affected by alcohol and are significantly associated with the risk of diabetic retinopathy [85]. The exclusive effect in men only may be explained by the protective effect of low or moderate alcohol consumption on the incidence of DR [86].

Since no study is exempt from unavoidable limitations. Ours has several limitations. Firstly, it included a higher number of female participants compared to males, this was mainly due to the very high prevalence rate among women, approximately double that of men, achieving a perfect balance might not have been feasible. To mitigate this bias, we conducted sex-stratified analysis to examine the risk factors for males and females separately. However, our findings highlight the importance of future research with a more balanced sex ratio to strengthen the generalizability of the results for both men and women with diabetes. Secondly, throughout the study, we used the notion of “sex” in the biological sense of the term, rather than “gender,” which is a socio-cultural construct. Comparing our results with those of other authors who have used the term “gender” in its socio-cultural dimension could potentially affect the generalizability of our findings. Therefore, in future research, questionnaires should include both “gender” and “sex.” Secondly, the presence of confounding factors alongside the risk factors associated with specific pathologies could introduce bias into the outcomes. For example, the literature suggests a higher risk of cataract occurrence after the age of 60. In future investigations, it may be advisable to focus on younger diabetic populations to address this issue.

Conclusion

The results of our study indicate a significant prevalence of diabetic multimorbidities within the population. To address this issue effectively, it is imperative to implement a combination of preventive and curative strategies. This should include efforts to combat risk factors such as hyperlipidemia, alcohol consumption, obesity, and sedentary lifestyles. Further research is warranted to better understand the mechanisms by which these factors operate and to develop strategies for controlling them, ultimately reducing diabetogenic environments. Achieving this goal can be realized through the establishment of educational programs and adherence to hygienic and dietary measures.

Author contribution IK: resources, SB: conceptualization, methodology, software, data analysis, writing, review and editing, validation; SD: methodology, writing, review and editing; AB: review and editing; MO: supervision and project administration.

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Data availability The data is available for a reasonable purpose.

Declarations

Conflict of interest The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Human rights statement The study was conducted in accordance with the principles of the Declaration of Helsinki 1964 and later versions. Participants were informed of the purpose of the study, the potential risks and benefits, and their right to withdraw at any time. They gave their informed consent before participating in the study. Those who volunteered signed the consent form and were included in the study. Participants' anonymity and privacy were respected at all times. Participants' personal data were anonymized before analysis. The data collected was stored in a secure location and will only be accessible to authorized persons. This research study was conducted retrospectively from data obtained for clinical purposes. We consulted with the Ministry of Health delegation in Nador who determined that our study did not require ethical approval. Official authorization to conduct the study was obtained.

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