

Risk factors for degenerative complications in patients with type 2 diabetes: nested case-control study 'epidiam' Morocco

Abstract

Aims: Our study aims to determine associated risk factors with complications of diabetes in patients with type 2 diabetes followed in primary care centers in Morocco.

Methods: We conducted a nested case-control study. Cases were type 2 diabetics patients who suffered from degenerative complication after diabetes diagnosis; controls were type 2 diabetics patients with no complications of diabetes at the time of inclusion in the cohort. The analysis was performed separately for women and men in order to determine the specificity of each sex factor.

Results: 732 patients with or without complications were identified. Retinopathy is the most frequent (41.2%) followed by diabetic neuropathy (28.4%) and cardiovascular complications (26.2%). For women, low economic level ($OR_{adj}=11.36$, 95% CI 5.59-23.25), forget the treatment ($OR_{adj}=3.42$, 95% CI 1.29-9.09), urban environment ($OR_{adj}=3.97$, 95% CI 0.04-0.17), very high level of stress ($OR_{adj}=2.94$, 95% CI 1.00-8.63), and overweight ($OR_{adj}=2.50$, 95% CI 1.12-5.53), remained significant with the risk of degenerative complications after adjustment. However, in unadjusted analysis for men, the low socioeconomic level and the patients without professional activities increased the degenerative complication risk. The patients with overweight [5.96 (95% CI: 1.61-22.10)], with dyslipidemia [3.09 (95% CI: 1.51-6.33)] and patients treated by a general physician [4.57 (95% CI: 1.24 - 16.82)] were a higher risk for degenerative complication.

Conclusion: These findings suggest that some risk factors of degenerative complication of type 2 diabetes are strongly linked with the Moroccan context. This study highlighted important areas for health care intervention and provided a reminder for vigilance when known risk factors for complications are present.

Keywords: type 2 diabetes, risk factor, degenerative complication, morocco, type 2 diabetes, epidemiology, disease, degenerative, patients, development

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Introduction

The magnitude of the global burden of morbidity and mortality from diabetes and its negative implications for human development and achievement of global development goals¹ are well documented. The vast majority of this burden is due to complications of diabetes and accounts for social substantial costs.^{2,3} Scientific research has demonstrated that resources for treating diabetes-related chronic complications are much bigger than resources allocated for management and compensation of the disease itself.⁴ Many of the complications of diabetes can be delayed or avoided by preventive measures and programs of support for this disease. Indeed, actions and preventive measures targeting determinants of diabetes complications impose their knowledge and identification. Some determinants are strongly related to cultural context, which are specific to each country. Multi-risk factor interventions, which include lifestyle changes and pharmacological therapy, have been shown to reduce the risk of diabetes complications by up to 50%.¹

In Morocco, a country in demographic, nutritional and epidemiological transition^{5,6} the prevalence of diabetes is always disquieting. Within a few years it raised from 6.3% to 6.6%.⁷ The latest national estimates this prevalence at 9% in people over 20years.⁸ In Morocco, to our knowledge, there is no analytical study to determine

the factors related to complications of type 2 diabetes. Our study aims to determine associated risk factors with complications of diabetes in patients with type 2 diabetes followed in primary care centers in Morocco.

Methodology

Study subjects

The present study was conducted as a nested case-control study in a cohort of type 2 diabetes patients. The recruitment of cases and controls is made from diabetic patients in the EpiDiaM cohort (Epidemiology Diabetes Morocco).

Cohort identification

The cohort EpiDiaM (epidemiology of diabetes in Morocco) is a prospective cohort study in a population of patients with type 2. We set up a monitoring every two years, the inclusion of patients in the cohort, took place from April 2012 to January 2013 month. We included 1,196 patients with type 2 diabetes in five primary health care centers and reference center of diabetes in Fez city.

Case/Control study

We recruited 366 cases and 366 controls.

The case: All diabetic patients in our cohort with one or more complications of diabetes (Macro-vascular, nephropathy, neuropathy and retinopathy) have been our target population of cases. We excluded patients who had complications before diagnosis of diabetes and patients with inability to determine the dates for the diagnosis of complication.

The control: All diabetic patients in our cohort with no complications represented our target population controls. Were defined as controls for this study; diabetic with no complications of diabetes at the time of inclusion in the cohort. Controls were matched to cases on age (± 5 years), sex and diabetes duration (± 5 years). We excluded patients with complications indeterminate situation (Figure 1).

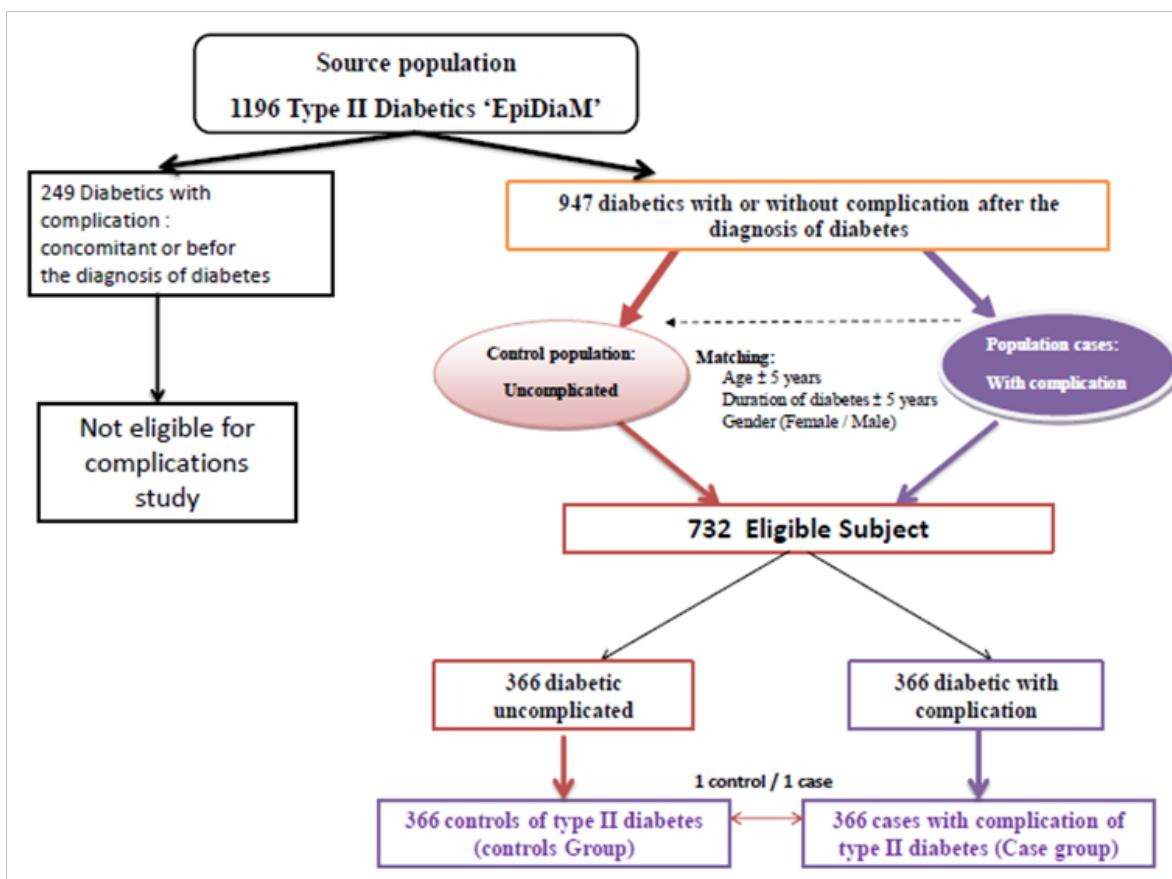


Figure 1 Flow chart of eligibility for the study and inclusion in the analysis.

Data collection

The collection of the information based on a questionnaire administered face to face by investigators and complemented by case medical of every patient. In addition to demographics characteristics we collected information on diabetes (history, treatment, monitoring), lifestyle (physical activities, smoking, alcohol consumption...) and complications of diabetes. Identification of complications was based on physician visits and data from medical records. In addition to the questionnaire, each patient's weight, height, and the blood pressure were measured.

Analytic plan

The descriptive phase was conducted at the beginning and summarized the quantitative variables as means with their standard deviations (SD) of 95% and qualitative variables as proportions (%) with confidence intervals (CI) 95%. In all our tests the matching of controls to cases was taken into account using conditional univariate and multivariate logistic regressions. The analysis was adjusted for all potential confounders. Sex is known as a modifier factor for association between risk factors and cardiovascular complications.^{9,10}

In addition some factors are specific to women (such as contraception) and other men especially in the Moroccan context (tobacco, alcohol ...). For these reasons the analysis was performed separately for women and men in order to determine the specificity of each sex factor. $P=0.05$ was the level of statistical significance. All analyses were performed using SPSS version 20.

Results

Population characteristics

We first identified a total of 1,196 diabetic patients from the EPIDIAM cohort study. The majority of the population was female (77.7%). Mean age was 57.5 ± 10.4 years and mean diabetes duration was 8 ± 6.60 years.

Characteristics of study subjects in nested case-control study

From the EPIDIAM cohort, 366 cases and 366 controls were recruited, as presented in Figure 1. The distribution of degenerative complications among the case is shown in Table 1. Retinopathy is the

most frequent (41.2%) followed by diabetic neuropathy (28.4%) and cardiovascular complications (26.2%).

Table 1 Distribution of Degenerative Complications of Type 2 Diabetes by Gender

Complication	CAS (N = 366)		
	N= 679	Women	Men
		N (%)	
Macro-Vascular	178 (26.2)	154 (86.5)	24 (13.5)
Retinopathy	280 (41.2)	222 (79.3)	58 (20.7)
Neuropathy	193 (28.4)	156 (80.8)	37 (19.2)
Nephropathy	28 (4.2)	24 (85.7)	4 (14.3)

Risk factors

In women, Table 2 shows the results of the unadjusted and adjusted analysis for women. In this unadjusted analysis, absence of health insurance (OR=1.45, 95% CI: from 1.02 to 2.08), unschooled patients (OR=1.61, 95% CI: from 1.04-4.95) and sleep during the day (OR=1.50, 95% CI 1.05 to 2.13) increased the risk of complications significantly. The very high stress level had a significant impact on

the degenerative complications risk (OR=3.23, 95% CI: 1.55 to 6.86). Dyslipidemia (OR=3.45, 95% CI 2.51 to 4.73), low socioeconomic level (OR=8.33, 95% CI: 4.58-12.98), urban residence (OR=6.80, 95% CI: 2.66 to 17.38), obesity (OR=2.01, 95% CI 21.23 to 3.27) and forget the treatment (OR=2.47, 95% CI 1.06 to 5.74) have been associated with a significantly higher risk to develop a degenerative complication. After multivariate adjustment, low economic level (OR_{adj}=11.36, 95% CI 5.59 - 23.25), forget the treatment (OR_{adj}=3.42, 95% CI 1.29 - 9.09), urban environment (OR_{adj}=3.97, 95% CI 0.04 - 0.17), very high level of stress (OR_{adj}=2.94, 95% CI 1.00 - 8.63), and overweight (OR_{adj}=2.50, 95% CI 1.12 - 5.53), remained significant with the risk of complications.

In men, the results concerning the unadjusted analysis for men are listed in Table 3. The low socioeconomic level and the patients without professional activities increased the degenerative complication risk with ORs, [3.03(95% CI: 1.41- 6.36)] and [1.29(95% CI: 1.04 - 1.60)], respectively. The patients with overweight [5.96(95% CI: 1.61 - 22.10)], with dyslipidemia [3.09(95% CI: 1.51- 6.33)] and patients treated by a general physician [4.57(95% CI: 1.24 - 16.82)] were a higher risk for degenerative complication. We have not been able to do a multivariate analysis for men. Due to lack of statistical power (low number of diabetic patients) conditions for statistical modeling was not satisfied.

Table 2 Distribution and Study of the Association Between all Risk Factors and Degenerative Complications Confused among Women at Morocco

Women Characteristics						
Case N=293	Control N=293		Crude OR	IC 95%	Adjusted OR*	IC 95%
Areas						
-Urban	287	258	6.8	2.66 - 17.38	3.97	1.08 - 14.58
-Rural	6	35	1	-	-	-
Socioeconomic level						
-Low	232	107	8.33	4.58 - 12.98	11.36	5.59 - 23.25
-Medium and High	61	186	1	-	-	-
Education						
-Yes	40	59	1	-	NA	-
-No	253	234	1.61	1.04 - 4.95	-	-
Profession						
-Active	6	12	1	-	NA	-
-Unactive	287	281	0.54	0.20 - 1.47	-	-
Social coverage						
-Yes	218	194	1	-	NA	-
-No	75	99	1.45	1.02 - 2.08	-	-
Smoking status						
-Non smoker	-	-	-	-	-	-
-Current smokers	-	-	-	-	-	-
-Former smokers	-	-	-	-	-	-
Alcohol						
-Non cosmuer	-	-	-	-	-	-
-Current Cosmuer	-	-	-	-	-	-
-Former Cosmuer	-	-	-	-	-	-

Table continued...

Women Characteristics						
Case N=293	Control N=293		Crude OR	IC 95%	Adjusted OR*	IC 95%
BMI Classes (Kg/m²)						
-]18.5-25[36	60	1	-	-	-
-]25-30[121	98	2	1.23 - 3.27	2.5	1.12 - 5.53
- 30<	134	134	1.65	1.01 - 2.69	2.09	0.96 - 4.53
Physical activity	37	24	1.68	0.95 - 2.97	NA	-
Sedentary lifestyle						
-≤1	73	47	1	-	NA	-
-] 1-2]	76	45	1.02	0.58 - 1.80		
-] 2-4]	95	50	1.15	0.69 - 1.91		
- 4 ≤	49	146	0.17	0.09 - 0.30		
Sleepy during the day	166	140	1.5	1.05 - 2.13	NA	-
Family history of diabetes	194	167	1.23	0.85 - 1.78	NA	-
Stress						
-Low	35	37	1	-	-	-
-Middle	118	157	0.76	0.43 - 1.33	0.51	0.21 - 1.22
-High	87	80	1.19	0.67 - 2.09	1.22	0.51 - 2.93
-Very High	53	17	3.23	1.55 - 6.86	2.94	1.00 - 8.63
Type the usual doctor						
-Special	11	17	1	-	-	-
-General	236	104	3.23	1.18 - 8.83		
-Both	36	14	4	1.21 - 13.20	NA	
-No one	10	7	2.35	0.51 - 10.76		
Forget Treatment	24	8	2.47	1.06 - 5.74	3.42	1.29 - 9.09
Dyslipidemia	79	27	3.45	2.51 - 4.73	NA	-

*Adjusted for Areas, Socioeconomic Level, Education, Social Coverage, BMI, Physical Activity, Sedentary Lifestyle, Sleepy During the Day, Stress, Type the Usual Doctor, Forget Treatment, Comorbidities Including Dyslipidemia

*Smoking Status in Male only (no woman was current or former smoker in our study).

CI, Confidence Interval, OR, Odds Ratio

Table 3 Distribution and study of the association between all risk factors and degenerative complications confused among men at Morocco

Men characteristics				
Case N=82	Control N=82		Crude OR	CI 95%
Areas				
-Urban	71	67	5	0.58 - 42.79
-Rural	2	6	1	-
Socioeconomic level				
-Low	43	25	3.03	1.40 - 6.36
-Middle High	30	48	1	-
Education				
-Yes	36	46	0.61	0.33 - 1.14
-No	37	27	1	-

Table continued...

Men characteristics				
Case N=82	Control N=82		Crude OR	CI 95%
Profession				
-Active	18	27	1	-
-Un active	55	46	1.29	1.04 - 1.60
Social coverage				
-Yes	39	28	1	-
-No	34	45	1.73	0.91 - 3.27
Smoking status				
-Non smoker	41	41	1	-
-Current smokers	11	13	0.75	0.26 - 2.18
-Former smokers	21	19	1.16	0.52 - 2.61
Alcohol				
-Non cosmuer	57	54	1	-
-Current cosmuer	1	5	0.21	0.02 - 1.86
-Former cosmuer	15	9	1.75	0.69 - 4.43
BMI Classes(Kg/m²)				
-]18.5-25[21	35	1	-
- [25-30[35	33	1.71	0.80 - 3.67
- 30<	16	5	5.96	1.61 - 22.10
Physical activity	14	12	1.222	0.50 - 2.94
Sedentary lifestyle				
-≤1	15	20	1	-
-] 1-2]	12	16	1.03	0.37 - 2.86
-] 2-4]	22	12	2.08	0.83 - 5.20
-] 4-6[24	13	1.08	0.53 - 2.81
Sleepy during the day	30	36	0.68	0.33 - 1.38
Family history of diabetes	39	36	0.95	0.53 - 1.71
Stress				
-Low	22	7	1	-
-Middle	27	43	0.16	0.05 - 0.53
-High	9	15	0.15	0.04 - 0.60
-Very High	15	8	0.48	0.13 - 1.81
Type the usual doctor				
-Special	7	14	1	-
-General	57	31	4.57	1.24 - 16.82
-Both	6	7	1.99	0.36 - 10.94
-No one	3	1	5.38	0.32 - 90.35
Forget treatment	7	12	0.5	0.17 - 1.46
Dyslipidemia	12	5	3.09	1.51- 6.33

CI, confidence interval; OR, odds ratio

Discussion

We conducted a case-control study nested in a cohort to determine the factors associated with degenerative complications of type 2 diabetes in Morocco.

For women, we observed that the low socioeconomic level was associated with a significant increasing on the risk of degenerative complications among women. Although its mechanism has not been completely clarified, the low socioeconomic level can be a responsible of development of complications of diabetes with type 2 through different and complex processes.¹¹ It was previously reported that poverty affects diabetes complications via barriers to medical care in low-income neighborhoods and healthy nutrition and exercise facilities.¹² In addition, there is an evidence confirming that mortality rates from diabetes have been raising among lower income Canadians.¹³ In Moroccan context, poor women, like those in other studies among low-income women,^{14,15} often put their families' needs and preferences before their own.

This study adds to this knowledge a better understanding that the choice between critically important priorities (such as purchasing food or medication and paying the rent) has implications not only for their diabetes management, but also for their basic survival as a whole. Hence, for these persons, balancing represents a complex dilemma that is fraught with stress.¹⁶ This explains the statistically significant association found after adjustment with the stress in our diabetics. However, higher levels of psychosocial stress may affect a person's socioeconomic status, use of medical services and overall health.¹⁷⁻²⁰ Surwit et al.²¹ showed that stress management training for one year was associated with a reduction significance of HbA1c. However, very anxious patients didn't obtain a reduction in HbA1c level.

Additionally, obesity is associated with increased risks for complications.²²⁻²⁴ This connection is maintained after adjustment with other risk factors, with risk multiplied by 2.5 in women. Obesity is an important modifiable risk factor for type 2 diabetes,²⁵ cardiovascular disease²⁶⁻²⁷ and renal failure.²⁸ Given this, it would be expected that obese people with long-standing type 2 diabetes are more likely to have sub-optimal glycemic control and higher rates of cardiac and renal disease than their lean counterparts.²⁹ In this context, women are more risky than men for various reasons. All of women were unemployed or housewives, inactive, therefore they get more likely to gain weight. Moreover, the cultural factor imposes yet often women to be overweight because they are more appreciated than the skinny ones.³⁰⁻³² In some regions of Morocco, especially the South, the weight of the woman is even seen as a competitive advantage increasing her chances of finding a husband.³² However, our analysis did not indicate a significant association between complication risk and physical activity.

Forgetting to take medications more than 4times appears to multiply the risk 3.4times among our diabetic women. Forgetfulness is related to patients' skills or their ability to take medications (unintentional), and the differences between intentional and unintentional non adherence depend on the belief about the necessity of treatment.³³⁻³⁴ So the belief of treatment necessity measures to enhance memory or to remind the patients about their medication are needed. This non observance of treatment among women may be due to low socioeconomic level and diabetes duration.

While the observed association between the area and complication risks was demonstrated in previous epidemiologic studies,^{35,36} the risk of degenerative complications is multiplied by 3.9 in women who

reside in urban areas. This may be due to the sedentary lifestyle as well as a reduced access to a healthy food in urban areas. This can be also explained by the large number of people surveyed in urban areas. In Morocco, the care of individuals living in rural areas is very low due to their remoteness from health centers.

For men, we have not been able to do a multivariate analysis. Due to lack of statistical power (low number of diabetic patients) conditions for statistical modeling was not satisfied. Data from the univariate analysis show that the low socioeconomic level, the patients without professional activities, the overweight, the dyslipidemia and patients treated by a general physician were a higher risk for degenerative complication. The information provided in this study can be used to target clinical practice toward prevalent complications where excess risk is greatest and can be used as inputs into long-term disease and economic modeling. These results will aid in understanding the current and future excess burden imposed by diabetes and its complications. These data, therefore, still need cautious interpretation. However, our data were from a large number of patients and represented what actually took place in clinical practice. To our knowledge, in Morocco our case-control study is the first to directly analyze the relationship between degenerative complication and all risk factors that may lead to the occurrence of these complications among Moroccan diabetics.

The major limitation of the current study is the fact that the study conducted in primary health care centers and referral center for diabetes in urban areas, which failed to take into account rural diabetics, patients who are not yet diagnosed or followed, and of course the category of patients who consult in the private sector. Another limitation, for men, we have not been able to do a multivariate analysis. Due to low number of men diabetic in our study. Despite this study's limitations, a large population database was used, allowing for excess risk assessment and generalizability of the results. Moreover, we were able to take into account several important potential confounders, such as age, sex and diabetes duration. Although the strength of the observed association and its persistence after adjusting for several important confounders suggest a possible relationship between exposure to risks factors and degenerative complication risk, the observational nature of the study precludes conclusions about causality. Further studies are needed to confirm our results.

Therefore, our study added an important knowledge of risk factors responsible for the occurrence of degenerative complications resulting in hospitalization or death. This study highlighted important areas for health care intervention and provided a reminder for vigilance when known risk factors for complications are present.

Author disclosures

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Conflict of interest

Author declares that there is no conflict of interest.

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