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Albuminuria in patients with young onset type 2 diabetes

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ABSTRACT

Introduction: Findings from several studies have indicated that patients with young onset diabetes (YOD) are more likely than those with late-onset diabetes (LOD) to have poor metabolic control and more diabetes-associated complications.
Objectives: This study was to assess assess the profile at admission and the evolution in a cohort of young patients presenting type 2 diabetes (T2D) and to study the influence of glycemic control on progression of albuminuria.
Patients and Methods: This is a prospective study. Inclusion criteria targeted patients who had T2D diagnosed before the age of 40 years and had been regularly followed in nephrology consultation for at least 36 months.
Results: A total of 121 patients met the inclusion criteria. Mean age at diabetes diagnosis was 39 ± 3 years and 64.5% were female. Mean body mass index (BMI) was 28.02 ± 4.47 kg/m^2. 22.3%, 57.9% and 19.8% had respectively, negative, micro- and macro-albuminuria. 22.3% were hypertensive, 36.4% had controlled diabetes and 14.9% had an estimated glomerular filtration rate (GFR) of <60 mL/min/m^2. At the end of follow-up, 27.3% were hypertensive, 24% had controlled diabetes, 27.3% had negative albuminuria, 17.4% showed rapid renal progression and cardiovascular events occurred in 12.4% of cases.
Conclusion: Control of blood pressure, glycemia and albuminuria remain difficult to achieve in adults with YOD type 2, thus exacerbating the renal and cardiovascular disease (CVD) risk.

Implication for health policy/practice/research/medical education:
Patients diagnosed with type 2 diabetes (T2D) under the age of 40 years are designated as having young onset diabetes (YOD) and its prevalence is increasing. They are more likely than those with late-onset diabetes (LOD) to have poor metabolic control and more diabetes-associated complications.
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Introduction

Diabetes afflicts nearly 382 million people worldwide, a proportion that will increase by 55% and is predicted to reach more than 592 million by the year 2035 (1). The majority of the 382 million people with diabetes are aged between 40 and 59 years and 80% of them live in low- and middle-income countries (1). Patients diagnosed with type 2 diabetes (T2D) under the age of 40 years are designated as having young onset diabetes (YOD) and its prevalence is increasing, especially in resource-poor countries, partly driven by the rising prevalence of obesity (2,3). Findings from several studies have indicated that patients with YOD are more likely than those with late-onset diabetes (LOD) to have poor metabolic control and more diabetes-associated complications (4,5). Diabetic kidney disease is usually seen in diabetic patients over the age of 40 years with a prevalence of 25% to 40% (6). The severity of progression of diabetes complications remains associated with the duration of diabetes evolution. This places the young T2D patients at high risk of kidney and cardiovascular diseases (CVDs) in the long term. What are the presenting and progressing characteristics of diabetic nephropathy (DN) and CVD in the young adult T2D patient?

Objectives

This study was to assess the profile at admission and the evolution in a cohort of young patients presenting

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Original

T2D and to study the influence of glycemic control on progression of albuminuria.

Patients and Methods

Study population

This is a prospective investigation started in January 2010 and carried out at the reference center for chronic diseases in Oujda, Morocco (Eastern Morocco). Inclusion criteria targeted individuals who had T2D that was diagnosed before the age of 40 years and had been regularly followed in nephrology consultation for at least 36 months. Rapid renal progression was defined as sustained decline in estimated glomerular filtration rate (eGFR) by the modification of diet in renal disease (MDRD) of more than 5 mL/min/1.73m^2/year. Cardiac events were defined by history of angina, myocardial infarction, heart failure and/or coronary revascularization. Excluded from the study were patients who had T2D diagnosed after the age of 40 years and who had other diseases than diabetes capable of altering renal function. We have identified three groups of patients according to the progression of albuminuria values at the end of the study (normo, micro and macro albuminuria), whatever the value of the baseline albuminuria.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The Ethics Committee of Morocco's Mohammed V University in Rabat approved the study protocol (University Mohamed V, Rabat). Verbal informed consent was required from all participants. The goals of the study were explained to participants and all of them accepted to participate and were assured consider the confidentiality of their individual information as well as the voluntary nature of participating in the study.

Statistical analysis

Data were analyzed using the SPSS version 13.0 (SPSS, Inc., Chicago, IL). Comparison of quantitative variables between three groups was performed using analysis of variance (ANOVA) if the variable was symmetrically distributed or the Kruskal–Wallis test if the variable was asymmetrically distributed. To determine which two of the three groups have a statistically significant difference, we used a post hoc analysis with the Bonferroni test. Comparison of qualitative variables between three groups was performed using the chi-square test. Comparison of qualitative variables between paired groups was performed using the chi-square test. Logistic regression was used to identify risk factors in multivariate analysis. Results were reported with odds ratio (OR) and 95% confidence interval (CI). All P values were two-sided and $P < 0.05$ was considered statistically significant.

Results

Out of 670 T2D patients followed regularly in nephrology clinic, 121 patients met the inclusion criteria. This represents 18.3% of T2D patients who were diagnosed with diabetes at less than 40 years. Mean age of 121 patients included at the time of diabetes diagnosis was 39 ± 3 years and 5.8%, 22.3% and 71.9% of them were respectively aged less than 30, 31–35 and 36–40 years at the moment of the diabetes diagnosis. 64.5% were of female gender. A family history of T2D was noted in 72.7% of cases. At the time of enrollment, body mass index (BMI) was 28.02 ± 4.47 kg/m^2, 26.4% were obese and 22.3%, 57.9% and 19.8% of cases had respectively, negative, micro- and macro-albuminuria. 22.3% were hypertensive, 36.4% had controlled diabetes ($Hb_{A1C} < 7\%$) and 14.9% had a glomerular filtration rate (GFR) estimated by the MDRD equation of <60 mL/min/m^2. At the end of follow-up, 27.3% were hypertensive, 24% had controlled diabetes, 27.3% had negative albuminuria, 17.4% showed rapid renal progression, 20.7% were taking more than two anti-hypertensive drugs, 37.2% had diabetic retinopathy and cardiovascular events occurred in 12.4% of cases. Table 1 shows the comparison of clinical and biological parameters between three groups of young T2D patients according to the evolution of albuminuria at the time of enrollment and at the end of the study. In multivariate analysis and adjusting for the duration of diabetes evolution, both admission albuminuria (OR: 0.96, CI: 0.94–0.98, $P = 0.007$) and male gender (OR: 0.14, CI: 0.03 –0.58, $P = 0.004$) were identified as risks for albuminuria in the patient with YOD. Positive albuminuria at the end of follow-up was observed in 64.1% vs. 88.4% ($P = 0.005$) respectively in the two groups, women and men. The mean duration of diabetes was 17.2 ± 49.1 vs. 16.8 ± 9.5 years ($P = 0.82$) respectively in the two groups, women and men. By comparing certain data between the men's group (n = 43) and women's group (n = 78), we noticed that the incidence of smoking was 46.5% vs. 0% ($P < 0.001$), the incidence of family history of diabetes was 80.8% vs. 58% ($P = 0.007$), the incidence of arterial hypertension history was 33.3% vs. 41.9% ($P = 0.23$). The mean BMI was 29.0 ± 4.5 vs. 26.1 ± 3.6 kg/m^2 and the annual mean values of Hb_{A1C} were 8.8 ± 1.7 vs. 8.5 ± 1.6% ($P = 0.34$) respectively for women and men.

Discussion

In Morocco, the prevalence of diabetes is estimated at 13.4% of the overall population aged 26 to 70 years and at 6.2% of the population aged 26 to 40 years (7). In our cohort, 18.3% of all diabetic patients followed were diagnosed with diabetes before the age of 40, of whom 90% were diagnosed between the ages of 31 and 40. The same prevalence (18%) has been found in a large Asian cohort, while other studies report much higher rates of prevalence reaching as high as 40% (8,9).

Very few studies have addressed the progression of diabetic kidney disease and even fewer the influence of glycemic control on albuminuria in young T2D patients. Independently of the duration of diabetes, patients with YOD had higher rates of diabetes complications and poorer glycemic control than did those with LOD. In the large Asian cohort, prevalence rates of chronic kidney

Table 1. Comparison of clinical and biological parameters between the three groups of patients according to the evolution of albuminuria

Characteristics (N= 121)	All patients (n=121)	Group 1 Normo-albuminuria (n= 33)	Group 2 Micro-Albuminuria (n= 69)	Group 3 Macro-albuminuria (n= 19)	*P* value
At baseline of the study					
Gender Male, n (%)	43 (35.5)	5 (15.2)	29 (42)	9 (47.4)	0.01
Age at diabetes diagnosis, years *	36.8 ± 3	36.5 ± 3	37 ± 3	36 ± 3	0.40
Duration of diabetes, years #	19 ± 9	14.5 ± 7 *	16 ± 9	21 ± 11*	0.03
BMI, kg/m^2 *	28.02 ± 4.47	27.2 ± 4.6	28.2 ± 4.2	28.6 ± 5.1	0.48
Family history of diabetes, n (%)	88 (72.7)	26 (78.8)	47 (68.1)	2 (10.5)	0.42
History of hypertension, n (%)	45 (37.2)	6 (18.2)	27 (39.1)	12 (63.2)	0.005
History of CVD (ischemic heart disease, peripheral vascular disease), n (%)	8 (6.6)	0	6 (8.7)	2 (10.5)	0.06
Smokers, n (%)	20 (16.5)	3 (9.1)	13 (18.8)	4 (21.1)	0.59
SBP, mm Hg *	135 ± 17	129 ± 17 *	134 ± 15	144 ± 19 *	0.01
DBP, mm Hg *	75 ± 10	73 ± 11	74 ± 10	79 ± 9	0.18
Arterial hypertension, n (%)	27 (22.3)	4 (12.1)	14 (20.3)	9 (47.4)	0.01
Albumin excretion rate, mg/day #	79 [38, 219]	26 [14, 50]	72 [54, 92]	621 [419, 1700]	<0.001
Estimated GFR by MDRD, mL/min/1.73m^2 *	93 ± 29	102 ± 23 *	98 ± 26 **	61 ± 23 * **	<0.001
Estimated GFR by MDRD <60 mL/min/1.73m^2, n (%)	18 (14.9)	0	6 (8.7)	12 (63.2)	<0.001
Hb_{A1C}, % *	9.0 ± 1.9	9.1 ± 2.0	9.0 ± 2.1	8.7 ± 1.8	0.84
Hb_{A1C} < 7%, n (%)	44 (36.4)	12 (36.4)	25 (36.2)	7 (36.8)	0.99
Total cholesterol, mg/dL *	194 ± 41	198 ± 41	194 ± 41	187 ± 10	0.66
LDL-cholesterol, mg/dL *	119 ± 34	121 ± 37	117 ± 35	117 ± 30	0.61
HDL-cholesterol, mg/dL *	46 ± 8	48 ± 7	46 ± 8	44 ± 21	0.18
Triglyceride, mg/dL *	133 ± 54	117 ± 43	140 ± 60	135 ± 48	0.15
Follow-up of the study					
Duration of follow-up, months *	36 ± 11	37 ± 11	38 ± 14	39 ± 13	0.54
Insulin use, n (%)	71 (58.7)	15 (45.5)	40 (58)	16 (84.2)	0.02
ACEi, ARBs use, n (%)	91 (75.2)	16 (48.5)	59 (85.5)	16 (84.2)	<0.001
Statin use, n (%)	33 (27.3)	3 (9.1)	23 (33.3)	7 (36.8)	0.02
Education by dietitian, n (%)	47 (38.9)	12 (36.3)	27 (39.1)	8 (42.1)	0.67
Diabetic retinopathy, n (%)	45 (37.2)	6 (18.2)	27 (39.1)	12 (63.2)	0.005
Diabetic neuropathy, n (%)	57 (47.1)	11 (33.3)	32 (46.4)	14 (73.7)	0.01
Cardiovascular events occurred, n (%)	15 (12.4)	1 (3.3)	11 (15.9)	3 (15.8)	0.11
Annual average of systolic blood pressure, mm Hg *	135 ± 20	128 ± 17 *	135 ± 18	145 ± 19 *	0.01
Annual average of diastolic blood pressure, mm Hg *	75 ± 9	73 ± 11	76 ± 9	77 ± 9	0.21
Arterial hypertension, n (%)	33 (27.3)	3 (9.1)	18 (26.1)	12 (63.2)	<0.001
Albumin excretion rate, mg/d#	33 [28, 134]	18 [13, 23]	68 [48, 114]	740 [420, 2200]	<0.001
Estimated GFR by MDRD mL/min/1.73m^2 #	91 ± 29	103 ± 22 *	96 ± 26 **	59 ± 27 * **	<0.001
Estimated GFR by MDRD <60 mL/min/1.73m^2, n (%)	20 (16.5)	1 (3)	7 (10.1)	13 (68.4)	<0.001
Rapid renal progression, n (%)	21 (17.4)	1 (3)	8 (11.6)	12 (66.7)	<0.001
End stage renal disease, n (%)	2 (1.7)	0	1 (1.4)	1 (5.3)	0.35
Annual average of Hb_{A1C}, % *	8.7 ± 1.6	8.3 ± 1.7	8.7 ± 1.6	9.2 ± 1.5	0.04
Hb_{A1C} < 7%, n (%)	29 (24)	9 (27.3)	17 (24.6)	3 (15.8)	0.63

Abbreviations: Hb, Hemoglobin; eGFR, estimated glomerular filtration rate; MDRD, modification of diet in renal diseases; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; DBP, diastolic blood pressure; hypertension defined as SBP>140 mm Hg and/or DBP >90 mm Hg; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index.

***** Variables expressed as mean ± SD (standard deviation); # variables expressed as median IQR (interquartile range). * or ** Difference statistically significant between two groups that designated by these symbols.

disease (CKD) and end stage renal disease (ESRD) were respectively 10% vs. 16% ($P<0.001$) and 1% vs. 1% ($P=0.78$) in patients with YOD and those with LOD, while glycemic control was better in patients with LOD than in those with YOD (42% vs 27% $P<0.001$) (8). In our series, 36.4% and 24% of patients with YOD had controlled diabetes respectively (Hb_{A1C} <7%) at the beginning and end of the study. Hillier et al studied a cohort of 1600 patients with YOD and after an average follow-up of 3.9 years; they found an incidence of micro albuminuria of 26.3% and an incidence of ESRD of 1.4% (10). In this study, the level of Hb_{A1C} was higher than in the YOD group than in the LOD group (8.7 ± 2.4 vs 8.1 ± 2.2 %, $P<0.001$) (10).

In a study conducted in Hong Kong, the authors studied 2066 patients with YOD and after a mean follow-up of 7.1 years, noted that at any given age at baseline, patients with young-onset diabetes had a higher incidence of both cardiovascular and renal events compared with those with LOD (11). Also noteworthy in the study, is that the

incidence of micro albuminuria, macro albuminuria, chronic kidney disease and ESRD, were respectively 23%, 13.4%, 4.6% and 0.6% at the start of the study. The Hb_{A1C} level was also higher in the YOD group than in the LOD group (7.8 ± 2 vs 7.6 ± 1.0 %, $P<0.001$) (11). In Japan, 40% of young type 2 diabetic patients developed overt proteinuria compared with 20% in type 1 diabetic patient after 30 years (12). In Caucasians, patients with YOD type 2 had a 20% increased hazard ratio for micro albuminuria compared with the LOD group (10). Al Saeed et al compared the prevalence of complications in 354 patients with T2D diagnosed between 15 and 30 years of age with that in a duration-matched cohort of 1062 patients diagnosed between 40 and 50 years, they found more severe albuminuria ($P=0.004$) in YOD than older onset diabetes (13).

We have found male gender to be a risk factor for albuminuria in patients with YOD type 2. Several hypotheses may explain this result; incidence of heavy smoking, poor treatment adherence and genetic predisposition.

Conclusion

Control of blood pressure, glycemia and albuminuria remain difficult to achieve in adults with YOD type 2, thus exacerbating the renal and CVD risk, a risk that is necessarily conditioned by the long duration of their diabetes. International recommendations concerning achievement of therapeutic goals do not distinguish between YOD patients and those with LOD. Do we need to be more demanding and strict in our approach to patients with YOD type 2?

Limitations of the study

The relatively small sample of patients was a limitation of the study.

Authors' contribution

YB; study design, data collection and manuscript drafting. RA; statistical analysis and manuscript re-viewing.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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