Prevalence of retinopathy in Caucasian type 2 diabetic patients from the South of Brazil and relationship with clinical and metabolic factors

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Abstract

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Diabetic retinopathy (DR) is a sight-threatening chronic complication of diabetes mellitus and is the leading cause of acquired blindness in adults. In this cross-sectional study, we investigated the prevalence of and the factors associated with DR in an analysis of 210 consecutive and unrelated Brazilian Caucasians with type 2 diabetes mellitus. Retinopathy was evaluated by ophthalmoscopy and/or biomicroscopy through dilated pupils. The relationship between clinical and metabolic variables and the presence of DR was assessed by logistic regression analysis. DR was detected in 99 of the 210 patients (47%). In the univariate logistic regression analyses, male sex, duration of diabetes, body mass index, glycated hemoglobin, C-peptide, LDL cholesterol, smoking, and albumin excretion rate were found to be associated with the presence of DR. However, the multiple logistic regression analysis showed that only duration of diabetes (odds ratio (OR) = 1.15, 95% CI = 1.09-1.22; P < 0.001), glycated hemoglobin (OR = 1.21, 95% CI = 1.01-1.46; P = 0.047) and albumin excretion rate >100 μg/min (OR = 12.72, 95% CI = 3.89-41.56; P < 0.001) were independently associated with DR. Although DR was found to be frequent among Brazilian type 2 diabetic patients, its prevalence was within the range observed in other Caucasian populations. Our findings emphasize the need for good glycemic control in order to prevent or delay the onset of DR, since the most well-known risk factors for the development of this complication in type 2 diabetes mellitus, such as duration of diabetes, glycated hemoglobin and albumin excretion rate were independently related to DR.

Diabetic retinopathy (DR) is a sight-threatening chronic complication of diabetes mellitus (DM) and is the leading cause of acquired blindness in adults, as reported by the American Diabetes Association (1). Up to 21% of patients with type 2 DM have retinopathy at the time of first diagnosis of diabetes, and most develop some degree of retinopathy over time (1). Duration of diabetes (1), hyperglycemia (2,3), high blood pres-

sure (3,4), and increased albumin excretion rate (AER) (5,6) have been identified as important risk factors for the onset and progression of DR in type 2 DM. However, epidemiological studies investigating the occurrence of DR in Brazilian type 2 diabetic patients are limited to the Southeast region (7).

The aim of the present study was to assess the prevalence of and the clinical and metabolic factors associated with DR in Caucasians with type 2 DM, from the State of Rio Grande do Sul in the South of Brazil.

A cross-sectional study was carried out on type 2 diabetic patients regularly attending the diabetes outpatient clinics at the Endocrinology Service of the Grupo Hospitalar Conceição, in Porto Alegre, located in the southernmost Brazilian State. Diagnosis of type 2 DM was based on the criteria of the American Diabetes Association (8). All patients with type 2 DM were invited to participate in a study investigating clinical and metabolic risk factors for diabetic complications. The present study refers to the analysis of 210 consecutive and unrelated patients (142 females and 68 males; mean age 58.7 ± 12.0; age range 28 to 87 years; mean duration of diabetes 10.5 ± 9.7 years) of European ancestry (mainly from Italy, Germany, Portugal, and Spain). All patients were born in Rio Grande do Sul, 89% lived in the metropolitan area of Porto Alegre and 11% in the rural area. Subjects from other ethnic groups were not included in the present study. The patients answered a standard questionnaire on clinical history and personal habits. The study protocol was approved by the Grupo Hospitalar Conceição Ethics Committee and all patients gave written informed consent to participate.

Hypertension was defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg, or was considered to be present if the patient was on treatment with antihypertensive drugs (9). Smoking was classified as "yes/no" (current and former smokers as opposed to subjects who had never smoked), and insulin therapy was defined as "yes/no" for regular use of insulin with or without oral hypoglycemic agents as compared to subjects who did not use insulin.

DR was assessed by ophthalmoscopy and/ or biomicroscopy through the dilated pupils by a physician specialized in retina (1), who had no knowledge of the patients' characteristics, and fluorescein angiography was obtained when indicated. DR was graded as absent, minimal, moderate, or severe retinopathy, as published elsewhere (10). For the purpose of the present study, the comparisons between the groups of patients were performed according to the presence or absence of DR, regardless of its levels of severity.

Fasting venous blood samples were obtained for the determination of glycated hemoglobin (HbA_1), creatinine, C-peptide, and plasma lipids. Twenty-four-hour urine samples were collected from 187 patients on at least two occasions for the measurement of AER. Glycated hemoglobin was measured by a colorimetric method (Labtest Diagnostica S.A., Lagoa Santa, MG, Brazil; laboratory reference range: 5.4-8.2%). Plasma creatinine concentrations were determined by a modified Jaffé reaction using an automated analyzer (Dade Behring Inc., Newark, NJ, USA). C-peptide levels were measured by radioimmunoassay (intra-assay coefficient of variation (CV) <10% and interassay CV <9%; Diagnostic System Laboratories Incorporation, Webster, TX, USA). Total plasma cholesterol, HDL cholesterol and triglycerides were measured by enzymatic methods using an automated analyzer (Dade Behring Inc.). LDL cholesterol was calculated using Friedewald's formula (LDL = total cholesterol - HDL - TG/5). Urinary albumin was determined with a double antibody radioimmunoassay (intra-assay CV <5% and interassay CV <3.5%; Diagnostic Products Corporation, Los Angeles, CA, USA).

Statistical analyses were performed using the SPSS package (SPSS for Windows, Version 8.0). Comparisons between groups were made using the unpaired Student t-test or the Mann-Whitney U-test. The χ^2 test was used to compare categorical characteristics between groups of subjects. A P value <0.05 was considered to be statistically significant. Logistic regression analyses were performed to assess the factors associated with the presence of DR as well as to control confounding factors.

Table 1 shows the clinical and metabolic characteristics of the patients regarding DR. Of the 99 patients with DR (which corresponds to 47.1% of the 210 patients analyzed), 36 (36.4%) had severe DR. The patients with DR had higher HbA_1 and LDL cholesterol levels, as well as a higher frequency of smoking. Their insulinopenia was more severe (lower C-peptide levels and more frequent use of insulin for diabetes treatment), and they were leaner than subjects without this complication. There was a trend toward a higher frequency of DR in men than in women (57 vs 42%, P = 0.057; χ^2 test with the Yates correction). The patients with DR had a longer duration of diabetes than those without it. In fact, the prevalence of DR increased from 17% at 5 years of duration of diabetes to 73% after 15 years of diabetes. Moreover, an AER >100 µg/min was much more frequent among the patients with retinopathy than among those without it (38 vs 5%, P < 0.001).

The multiple regression analysis model was constructed using the factors significantly associated with the presence of retinopathy in the univariate analyses, i.e., male sex (P = 0.047), duration of diabetes (P < 0.001), body mass index (P = 0.030), HbA_1 (P = 0.012), C-peptide (P = 0.015), LDL cholesterol >3.59 mmol/l (P = 0.026), smoking (P = 0.033), and AER (P < 0.001, for patients with AER >100 µg/min as compared to those with AER <20 µg/min).

The factors that remained statistically and independently associated with DR in the multiple logistic analysis after adjustment for sex and age were duration of diabetes, HbA_1 levels and AER, as shown in Table 2. Interaction effects among the variables were not significant.

DR was very frequent in our cross-sectional study. Yet its prevalence was somewhat higher than that observed in Caucasians with type 2 DM from the United States (39%) and from South Africa (41%) (11,12), and lower than that found in Caucasians from New Zealand (60%) (13). Most pa-

Table 1. Clinical and laboratory characteristics of patients with type II diabetes mellitus with and without diabetic retinopathy.

Variable	Without retinopathy	With retinopathy	P
Number (male/female)	111 (29/82)	99 (39/60)	0.057
Age (years)	57.5 ± 13.1	59.9 ± 10.6	
Duration of diabetes (years)	6.6 ± 7.5	14.9 ± 10.1	<0.001
Glycated hemoglobin (%)	9.8 ± 2.3	10.6 ± 2.2	0.010
Smoking (%)	28.8	43.4	0.039
Hypertension (%)	59.5	68.7	
Systolic blood pressure (mmHg)	136 ± 19	137 ± 23	
Diastolic blood pressure (mmHg)	85 ± 10	84 ± 10	
Body mass index (kg/m²)	30.7 ± 6.2	28.9 ± 4.0	0.016
Creatinine (µmol/l)	77 ± 24	90 ± 39	0.002
C-peptide (nmol/l)	1.07 ± 0.68	0.76 ± 0.58	0.006
Insulin therapy (%)	21.6	51.5	<0.001
Total cholesterol (mmol/l)	5.54 ± 1.12	5.91 ± 1.43	0.050
HDL cholesterol (mmol/l)	1.19 ± 0.60	1.06 ± 0.28	
LDL cholesterol (mmol/l)	3.54 ± 1.05	3.99 ± 1.30	0.014
Triglycerides (mmol/l)	1.55 (0.29-16.59)	1.56 (0.41-16.24)	
AER >100 µg/min (%)	4.9	38.1	<0.001

Data are reported as mean ± SD or as %. Triglyceride values are reported as median and range. The groups were compared by the unpaired Student t-test, the Mann-Whitney U-test or the χ^2 test.

Table 2. Relationships between various clinical factors and the presence of diabetic retinopathy.

Variable	OR	95% CI	P
Male sex	1.40	(0.56-3.49)	
Age (years)	0.98	(0.94-1.02)	
Duration of diabetes (years)	1.15	(1.09-1.22)	<0.001
Glycated hemoglobin (%)	1.21	(1.01-1.46)	0.047
AER >100 µg/min*	12.72	(3.89-41.56)	<0.001

OR = odds ratio; 95% CI = 95% confidence interval; AER = albumin excretion rate.
*P < 0.001 compared to patients with AER <20 µg/min (logistic regression analysis).

tients had never been examined in order to assess retinopathy and many of them were not aware of the risk of visual dysfunction.

Duration of diabetes and hyperglycemia are two well-known risk factors for the development of DR (1-3,6,7,14-17). In our study, patients with retinopathy had a longer duration of diabetes and more severe diabetes than patients without it, as indicated by a lower body mass index, a higher frequency of insulin therapy, higher HbA$_1$ levels, lower C-peptide levels, and a higher AER. Since these metabolic factors, which have been shown to be individually related to retinopathy, are correlated with one another and reflect poor metabolic control, only glycated hemoglobin, duration of diabetes and AER remained independently associated with the presence of retinopathy in the final analysis.

Both proteinuria and macroalbuminuria have been related to the development of DR in type 2 DM (5,6,18). In the present study, an AER >100 µg/min was strongly associated with the presence of DR, providing further evidence that once a complication has been established, glycemic control can be fundamental in delaying or avoiding the onset of other complications.

Although the clinical trial conducted by the UK Prospective Diabetes Study Group (3,4) and the Hoorn study (16) have shown that hypertension is a serious risk factor for the onset and the progression of DR in type 2 DM, other studies have found no relation-ship between this complication and high blood pressure (15,17,19), as was also the case in the present study. Even if hypertension were associated with retinopathy, we would not find this association, because the two groups of patients (with and without retinopathy) presented similar mean levels of systolic and diastolic blood pressure that could be attributed to the treatment with antihypertensive drugs, since 54.1% of the patients without retinopathy use some medication to control blood pressure versus 54.6% of the patients with retinopathy.

DR was present in approximately half of the patients with type 2 DM. This high frequency emphasizes the need to screen patients with type 2 DM for the detection of DR in the diagnosis of diabetes. However, the frequency of this complication may be restricted to the patients studied in the present investigation and cannot be extended to all diabetic patients. To our knowledge, this is the first study reporting on the prevalence of and the factors associated with DR in type 2 diabetic patients, in the South of Brazil. Moreover, our findings contribute to emphasize the need for good glycemic control in order to prevent or delay the onset of DR, since duration of diabetes, glycated hemoglobin and AER were independently related to DR. In conclusion, DR is a serious diabetic complication and public health strategies are required in order to reduce its risk factors and decrease its prevalence.

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