Moderate-to-Severe Diabetic Retinopathy Is More Prevalent in Mexico City Than in San Antonio, Texas

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OBJECTIVE — To compare the prevalence of diabetic retinopathy (DR) between low-income Mexicans from Mexico City and Mexican-Americans from San Antonio, Texas.

RESEARCH DESIGN AND METHODS — We designed a cross-sectional population-based study in low-income neighborhoods of Mexico City and San Antonio. The men and nonpregnant women included in the study had NIDDM and were between 35 and 64 years of age. Ophthalmologic evaluation was performed in 414 patients, 204 in San Antonio and 210 in Mexico City. Seven field standard stereophotographs of each eye were obtained, adapting the Early Treatment Diabetic Retinopathy Study protocol, and graded at the Fundus Photograph Reading Center of the University of Wisconsin.

RESULTS — Early nonproliferative DR occurred in 37 (17.6%) and 39 (19.1%) patients in Mexico City and San Antonio, respectively. Moderate-to-severe nonproliferative DR occurred in 55 (26.2%) and 37 (18.1%) patients in Mexico City and San Antonio, respectively, and proliferative DR occurred in 12 (5.7%) and 7 (3.4%) patients in Mexico City and San Antonio, respectively. Using univariate and multivariate logistic regression analysis with DR as the dependent variable, age, duration of disease, and fasting glucose concentration were positively and significantly associated with retinopathy, whereas city, systolic blood pressure, and other selected metabolic variables were not. We defined moderate-to-severe DR to include the categories of moderate-to-severe nonproliferative and proliferative DR. For this combined category, Mexico City patients with diabetes had a significantly higher prevalence ($P < 0.01$) than those from San Antonio when analyzed by multiple logistic regression analysis (odds ratio for Mexico City/San Antonio, 1.72; 95% CI 1.10–2.70).

CONCLUSIONS — Overall prevalence of DR is similar in both cities. However, moderate-to-severe DR is significantly higher in Mexico City.

Diabetic retinopathy (DR) is one of the leading causes of preventable blindness among adults (1). Since it has been proven that timely laser surgery can reduce the risk of visual loss by at least 50% (2,3), case ascertainment is clearly an urgent public health priority, particularly in high-risk populations.

Prevalence of type II diabetes varies in different countries and ethnic groups. It is now well established that certain ethnic groups are more susceptible to type II diabetes than others (4).

We found that low-income inhabitants of Mexico City have a high prevalence of type II diabetes (5), and the prevalence of DR is also high in this population (6).

Also, Mexican-Americans living in San Antonio, Texas, have an approximately threefold higher prevalence of type II diabetes and a more than twofold higher prevalence of DR, compared with non-Hispanic whites (7). In contrast, another study of Hispanic origin population reported no excess in the prevalence of DR (8).

The purpose of this study is to compare the prevalence of DR between low-income Mexicans from Mexico City and low-income Mexican-Americans from San Antonio. We hypothesized that these two populations would have a similar prevalence of DR.

RESEARCH DESIGN AND METHODS

— Data from San Antonio were taken from two cross-sectional surveys. The first cross-sectional survey was out from 1979 to 1982 and the second from 1984 to 1988. Households were randomly sampled from three types of neighborhoods, low- and middle-income neighborhoods and high-income suburbs. All 25- to 64-year-old men and nonpregnant women residing in the selected households were considered eligible for the study. Mexican-Americans were defined as individuals whose ancestry and cultural traditions derived principally from a Mexican national origin (9). Subjects with diabetes from both phases were recontacted and asked to participate in a diabetic complication examination.

Because the Mexico City survey involved only 35- to 64-year-old individuals living in a low-income neighborhood, the San Antonio data presented in this paper are restricted to the same age range (35–64 years) and to residents of the low-income San Antonio neighborhood.

A low-income area of Mexico City was selected for the study. The study site consisted of six neighborhoods, each one corresponding to one census tract. A complete household enumeration was performed in each neighborhood. Eligible individuals were men and nonpregnant women between 35 to 64 years of age. Once these individuals were identified, a home inter-

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DR, diabetic retinopathy; ETDRS, Early Treatment of Diabetic Retinopathy Study; FPRC, Fundus Photography Reading Center; OR, odds ratio.

view was attempted for each eligible subject.

The protocol and survey procedures were approved by the Institutional Review Board of the University of Texas Health Science Center in San Antonio and the Centro de Estudios en Diabetes in Mexico City. All subjects gave informed consent.

At both study sites, height, weight, subscapular and triceps skinfolds, waist and hip circumferences, systolic (1st phase), and diastolic blood pressure (5th phase) were measured as previously described (10), using the same protocols and following the same procedures. In Mexico City, before the beginning of the study, a joint training course was conducted to assure that the anthropometric and physiological measurements were performed in a standardized way at both study sites.

Participants were seen the morning after a 12-h fast. Height and weight were measured on a clinical scale. Subjects wore an examining gown without shoes. A metallic tape was used to measure the waist and hip circumferences. The umbilicus was used as a landmark for the former and the greater trochanter for the latter. Skinfolds were measured using a Lange skinfold caliper. The subscapular skinfold was measured at the inferior angle of the right scapula, and the triceps skinfold was measured at the mid portion of the right triceps muscle. BMI was calculated as weight (in kilograms) per height (in meters) squared, and centrality index was calculated as the ratio of subscapular to triceps skinfold. Upper versus lower body fat predominance was assessed by waist-to-hip circumference ratio (11).

Blood pressure measurements were performed using a random zero sphygmomanometer (Hawksley Gelman, London, U.K.) following the Hypertension Detection and Follow-Up Program protocol (12). Blood pressure was measured in the right arm of the seated subject after 5 min of rest. Blood pressure was determined three times, and the mean of the last two values was defined as the patient's blood pressure. The cuff size was determined by the patient's arm dimension. The staff that performed the measurement was trained in the technique by certified personnel. For the analysis presented in Table 4, the distribution of systolic blood pressure was divided into quartiles.

The techniques used and our laboratory methods have been published previously (13). A standard oral glucose tolerance test (75-g glucose load) was performed, and diabetes was diagnosed according to World Health Organization criteria (14). Glucose sum was calculated as the sum of fasting and 2-h glucose values. The glucose sum distribution was divided into quartiles for the analysis shown in Table 4. Individuals who reported a history of diabetes and who were under treatment with insulin or oral antidiabetic medications were considered to have diabetes, regardless of plasma glucose values. All the diabetic patients taking insulin with an onset of disease at <30 years of age and a BMI <30 kg/m^2 were considered possibly to have type I diabetes and were excluded from the analyses. Noninsulin takers were considered to have type II diabetes. The duration of disease was calculated as current age (recorded at the time of the complication examination) minus self-reported age at diagnosis of diabetes. Duration was divided in four categories for the analysis presented in Table 4.

Table 1—*Prevalence and severity of DR in Mexico City and San Antonio*

Grade of retinopathy	Mexico City		San Antonio	
	n	% (95% CI)	*n*	% (95% CI)
None	106/210	50.5 (43.72–57.24)	121/204	59.3 (52.57–66.05)
Early nonproliferative	37/210	17.6 (12.47–22.77)	39/204	19.1 (13.72–24.52)
Moderate to severe nonproliferative	55/210	26.2 (20.24–32.17)	37/204	18.1 (12.85–23.43)
Proliferative	12/210	5.7 (2.57–8.85)	7/204	3.4 (0.93–5.93)

Data are *n* or % (95% CI).

At both study sites, funduscopic examination of the retina was performed by a retina specialist using both direct and indirect ophthalmoscopy after dilation of the pupil. In both cities, stereoscopic fundus photographs of seven standardized fields of each eye were obtained using procedures adapted from the Early Treatment of Diabetic Retinopathy Study (ETDRS) (15). Before the beginning of the study in Mexico City, a certified fundus photographer and trainer from the Fundus Photography Reading Center (FPRC) of the Department of Ophthalmology of the University of Wisconsin traveled to Mexico City and carried out a 3-day training program during which two ophthalmologists received training in the technique of fundus photography according to ETDRS protocol (15). Mounted photographs were mailed to the FPRC. Slides were graded for quality first; only sets of acceptable photographic quality were graded. The analyses presented in this paper were based on the stereo retinal photographs graded using a modification of the modified Airlie House Classification (16). Retinopathy level 0 was coded as no retinopathy, levels 15–30 were coded as early nonproliferative, levels 40–50 as moderate-to-severe nonproliferative, and levels 60–80 as proliferative. When findings differed between the right and left eyes, the retinopathy grade used to classify the patient was based on the more severely affected eye.

Statistical analyses were performed using SYSTAT and LOGISTIC. Comparisons were made using one-way analyses of variance for continuous variables and multiple logistic regression for dichotomous variables (17,18).

RESULTS — The population of the six study sites in Mexico City was 15,532. Of these, 3,505 (22.6%) were found to be age eligible. Home interviews were obtained on 2,810 (80.2%) subjects. Physical and laboratory exams were obtained on 2,282 (81.2%) individuals. The total number of subjects with diabetes was 304 (122 men and 182 women). Between the first examination and the complication examination, 8 had died and 12 had changed their address. A final cohort of 284 was left. We were able to locate and perform full ophthalmologic evaluations on 210 (73.94%) of these individuals (83 men and 127 women).

In the San Antonio Heart Study, 407 subjects with type II diabetes were identified, 191 in phase I and 216 in phase II. Nine subjects from phase I died, and ten subjects were considered to have type I diabetes and were excluded from the analysis. Thus, 388 individuals were available for the complication examination. The response rate to this examination in Mexican-Americans was 257/320 (80.3%). To make the two groups comparable, we considered of these only Mexican-Americans residing in the low-income neighborhood

Table 2—*Comparison of the clinical and metabolic characteristics of patients with and without diabetic retinopathy in both cities*

	Any retinopathy			No retinopathy		
	Mexico City (n = 104)	San Antonio (n = 83)	P value	Mexico City (n = 106)	San Antonio (n = 121)	P value
Men	46 (44.2)	28 (33.7)	0.22	37 (34.9)	34 (28.1)	0.22
Women	58 (55.8)	55 (66.3)	0.24	69 (65.1)	87 (71.9)	0.24
Duration (years)*						
≤10	68 (65.4)	53 (63.9)	—	98 (92.5)	113 (93.4)	—
>10	36 (34.6)	29 (34.9)	0.92	7 (6.6)	8 (6.6)	0.99
Age (years)	50.3 ± 2.6	55.3 ± 7.3	0.019	50.4 ± 2.0	51.0 ± 9.4	0.716
Age at diagnosis (years)	42.9 ± 8.8	46.4 ± 10.8	0.016	47.1 ± 8.1	48.4 ± 9.3	0.265
Systolic blood pressure (mmHg)	131.0 ± 8.6	128.1 ± 15.7	0.205	129.4 ± 6.7	127.5 ± 15.1	0.007
Diastolic blood pressure (mmHg)	74.0 ± 9.8	73.7 ± 9.0	0.786	76.1 ± 10.3	75.6 ± 9.9	0.698
BMI (kg/m²)	27.9 ± 4.2	31.1 ± 6.3	0.001	29.9 ± 4.5	32.8 ± 6.2	0.001
Fasting glucose (mg/dl)	225.8 ± 83.0	200.0 ± 66.8	0.025	153.5 ± 65.3	160.5 ± 61.3	0.389
2-h postglucose (mg/dl)	299.2 ± 125.8	365.4 ± 95.2	0.003	273.3 ± 80.1	296.0 ± 87.1	0.106
Cholesterol (mg/dl)	207.1 ± 44.9	221.8 ± 45.8	0.030	197.9 ± 44.9	203.9 ± 43.0	0.311
Triglycerides (mg/dl)	247.9 ± 129.8	196.0 ± 94.6	0.339	257.6 ± 209.0	185.7 ± 93.0	0.126
HDL (mg/dl)	32.6 ± 7.6	42.9 ± 12.9	0.001	33.0 ± 9.9	40.6 ± 10.2	0.001
LDL (mg/dl)	131.5 ± 40.2	142.5 ± 41.9	0.076	125.8 ± 38.8	127.1 ± 35.7	0.760

Data are n (%), P, or means ± SD. *Total number of cases and the percentage do not add up due to missing values.

and in the age range of 35–64 years, yielding a total of 204 subjects.

A total of 104 (49.5%) subjects in Mexico City and 74 (36.3%) in San Antonio were taking oral agents. There were only 4 (1.9%) on insulin in Mexico City and 26 (12.8%) in San Antonio.

Table 1 shows the prevalence and severity of DR by city. There was no DR in 106 (50.5%) patients in Mexico City and 121 (59.3%) patients in San Antonio. We found early nonproliferative DR in 37 (17.6%) patients in Mexico City and 39 (19.1%) patients in San Antonio. There was moderate-to-severe nonproliferative DR in 55 (26.2%) patients in Mexico City and 37 (18.1%) patients in San Antonio. We found proliferative DR in 12 (5.7%) patients in Mexico City and 7 (3.4%) patients in San Antonio.

Table 2 presents a comparison of the clinical and metabolic characteristics of patients from the two cities who had any level of DR, compared with those who had no DR. Some clinical and metabolic variables were found to be significantly different among patients with and without DR between cities. However, in univariate logistic regression (with DR as the dependent variable) adjusted for age, sex, and duration, these differences did not reached statistical significance (Table 3).

Contingency tables were constructed to compare the risk by city of any grade of retinopathy with no retinopathy. We also created a category that we called moderate-to-severe retinopathy, which consisted of moderate-to-severe nonproliferative and proliferative combined, and compared this category to the other two categories combined (i.e., no retinopathy and early nonproliferative). The group from Mexico City had an increased risk of any retinopathy relative to the group from San Antonio (odds ratio [OR], 1.43; 95% CI 0.95–2.15), although this difference did not reached statistical significance.

The Mexico City patients had an increased risk of moderate-to-severe retinopathy relative to early nonproliferative or no retinopathy (OR, 1.70; 95% CI 1.07–2.72), which was statistically significant (P = 0.01). This difference did not appear to be attributable to differences in diabetic control between the cities, since

Table 3—*Logistic regression analysis for any level of diabetic retinopathy for Mexico City and San Antonio*

Risk factor	n	OR	95% CI	City effect P value
BMI (kg/m²)	185/411	0.95	0.91–0.99	0.967
Systolic blood pressure (10 mmHg difference)	185/411	0.99	0.87–1.13	0.481
Diastolic blood pressure (10 mmHg difference)	185/411	0.90	0.69–1.14	0.467
High blood pressure (present/absent)	186/412	0.62	0.36–1.06	0.358
Fasting glucose (10 mg/dl difference)	181/404	1.11	1.07–1.14	0.392
2-h postglucose (10 mg/dl difference)	107/276	1.05	1.03–1.08	0.075
Total cholesterol (5 mg/dl difference)	182/404	1.04	1.01–1.07	0.212
HDL (5 mg/dl difference)	181/401	1.04	0.93–1.17	0.254
LDL (5 mg/dl difference)	179/398	1.04	1.01–1.07	0.278

n represents the number of subjects with retinopathy over the total number of subjects. Univariate logistic regression was adjusted for age, sex, duration of diabetes, and city. Dependent variable was DR.

Table 4— *ORs and 95% CIs for risk factors for any retinopathy and moderate-to-severe retinopathy by multiple logistic regression analysis*

	Any retinopathy			Moderate to severe retinopathy		
	OR	95% CI	*P* value	OR	95% CI	*P* value
City (Mexico City/San Antonio)	1.45	0.97–2.16	0.068	1.72	1.10–2.70	0.018
Duration of diabetes (years)						
≤1	1.00	—		1.00	—	
>1–≤3	2.13	1.01–4.49	0.046	3.09	0.99–9.66	0.053
>3–≤10	3.75	1.84–7.65	0.003	10.47	3.71–29.54	0.000
>10	9.25	3.57–23.98	0.000	31.42	9.76–101.12	0.000
Glucose sum						
<350	1.00	—		1.00	—	
≥350–<450	0.89	0.40–2.01	0.788	0.78	0.25–2.42	0.665
≥450–<600	2.97	1.39–6.35	0.005	3.20	1.22–8.42	0.018
≥600	4.88	2.21–10.74	0.000	3.51	1.32–9.35	0.012
Age (10-year intervals)	1.52	1.19–1.94	0.001	1.45	1.10–1.94	0.009
Systolic blood pressure						
<115	1.00	—		1.00	—	
≥115–<130	0.98	0.47–2.04	0.953	1.29	0.51–3.27	0.586
≥130–<150	1.11	0.51–2.41	0.784	1.56	0.60–4.06	0.360
≥150	2.60	0.87–7.74	0.087	2.42	0.68–8.70	0.174

Glucose sum was calculated as the sum of fasting and 2-h glucose values.

there were no consistent glucose differences between the two cities, as shown in Table 2.

To elucidate the interrelationships among previously reported risk factors for retinopathy, multiple logistic regression stratified analyses were performed. The dependent variable was either any retinopathy or moderate-to-severe retinopathy. The predictor variables were city, age, sex, duration of disease, systolic blood pressure, and glucose sum. Table 4 shows these results.

For both dependent variables, age, duration of disease, and glucose sum were positively and significantly associated with retinopathy, whereas systolic blood pressure was not. As the predictor variable, city was positive and significantly associated with moderate-to-severe diabetic retinopathy (OR, 1.72; 95% CI 1.10–2.70; $P < 0.01$).

CONCLUSIONS — For this investigation, every effort was made to ensure methodological comparability between the two cities. Anthropometric and physiological variables were measured using the same protocol at both study sites. All laboratory procedures were performed in the same laboratory (San Antonio). Fundus photographs were sent to the same center for grading using the same criteria.

We have demonstrated that any level of DR is higher in Mexican patients, although this difference was only of borderline statistical significance ($P = 0.07$). However, for moderate-to-severe DR, Mexican subjects with diabetes appear to be at higher risk. Although the results for any retinopathy were only of borderline statistical significance, they are nevertheless consistent with the results for moderate-to-severe retinopathy, since the point estimate of the ORs (Mexico City/San Antonio) are both >1.0 and similar (Table 4) in magnitude. The lack of statistical significance may be attributable to the introduction of noise in the any-retinopathy analysis, because the hallmark lesion of early nonproliferative retinopathy, the microaneurysm, is not necessarily specific for diabetes, since it can be caused by other conditions different from diabetes.

Since Mexican-Americans have a higher risk for both diabetes and DR, compared with non-Hispanic whites, we may infer that Mexicans with diabetes are also at higher risk, compared with non-Hispanic whites. Also, like Mexican-Americans, Mexicans may be considered to be in "double jeopardy" (7), since they have both an increased risk of diabetes and, thus, an increased risk of DR.

Another population of Hispanic origin has been studied using the same methodology (8). In this group of patients, the prevalence of DR was not significantly higher than non-Hispanic whites. It is difficult to explain this apparent discrepancy. We believe, however, that the prevalence of DR, particularly the moderate-to-severe form, is high among Mexican patients with diabetes, since this is the general perception of most Mexican ophthalmologists.

One possible explanation for the greater severity of diabetic retinopathy in Mexico City compared with San Antonio patients with diabetes might be less access to health care, resulting in delayed diagnosis in the Mexico City population. If this were the case, one might expect more retinopathy in newly diagnosed cases from Mexico City than in newly diagnosed cases from San Antonio. This was, in fact, what was observed (prevalence of any retinopathy in newly diagnosed cases, 21/164 [32.8%] from Mexico City vs. 14/77 [18.2%] from San Antonio; $P = 0.071$). On the other hand, the ratio of newly to previously diagnosed cases was lower in Mexico City (64:146) than in San Antonio (77:127), suggesting no delay in diagnosis. This latter difference, however, was not statistically significant. Harris et al. (19) have suggested back-extrapolating the linear relationship between retinopathy and disease duration to the time when retinopathy prevalence is estimated to be zero to form an estimate of the time of disease onset. When this technique was applied to the present data set, there was no evidence that Mexico City patients with diabetes were, on average, diagnosed later in the course of their disease, compared with San Antonio patients.

It is possible that the prevalences of DR observed in this ethnic group might be the

result of the full expression of a genetic susceptibility catalyzed by chronic poor metabolic control (20). Since it is now known that effective metabolic control reduces the appearance and progression of DR (21), every effort should be made to ameliorate this severe public health problem.

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