Diabetes and Diabetic Retinopathy in a Mexican-American Population

Proyecto VER

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OBJECTIVES — The prevalence rate of diabetes is probably higher in Hispanics than in Caucasians, although there is controversy about differences in the risk of diabetic retinopathy. The purpose of the study is to determine the prevalence rates of diabetes and diabetic retinopathy in a population-based study of Hispanics aged ≥40 years.

RESEARCH DESIGN AND METHODS — Proyecto VER is a random sample of Hispanic populations aged ≥40 years in Arizona. A total of 4,774 individuals (71.6% of the eligible sample) completed the examinations. Diabetes was defined as self-report of a physician diagnosis or HbA_{1c} value of ≥7.0%. Diabetic retinopathy was assessed on stereo fundus photographs of fields 1, 2, and 4.

RESULTS — The prevalence rate of diabetes in the Hispanic community (individuals ≥40 years of age) was 22%. The prevalence rate of diabetic retinopathy (DR) was 48%; 32% had moderate to severe nonproliferative and proliferative retinopathy. DR increased with increasing duration of diabetes and increasing level of HbA_{1c}. The prevalence rate of DR-like changes in the sample of individuals without diabetic retinopathy was 15% and was not associated with hypertension, systolic blood pressure, or diastolic blood pressure.

CONCLUSIONS — The prevalence rate of diabetes in this population of Hispanics is high, almost twice that of Caucasians. The prevalence rate of DR is high but similar to reports in a Caucasian population. The prevalence rate of 9% moderate to severe retinopathy in the newly diagnosed group suggests that efforts to improve detection and treatment of diabetes in Hispanics may be warranted.

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In the U.S., the Hispanic population is the second largest minority group and, if the current trends continue, it will become the largest minority group in this century (1). This trend has led to considerable interest in the health and well-being of this population, which has ramifications for provision and utilization of health services. Several studies have pinpointed, in particular, the high prevalence rate of diabetes among Hispanics of Mexican origin (2–6). The prevalence rate in adults varies from 10–24% but is generally 2- to 2.5-fold higher in Mexican-Americans than in non-Hispanic whites (2–4,6,7). Mexican-Americans with diabetes seem to have more severe hyperglycemia as well, indicating poorer control (8).

However, there are conflicting reports about the prevalence rate of diabetic retinopathy (DR) in Mexican-Americans with diabetes; one study reported no greater risk compared with non-Hispanic whites, whereas others reported twofold or higher risk (9–11) The conflicting prevalence rates from these populations are unlikely to be due to differences in the definition of retinopathy, because fundus photographs were graded for all three studies by the same center in Wisconsin. In part, the discrepancies may be due to the smaller numbers in the San Luis Valley study (n = 187) and San Antonio Heart Study (n = 258). In the National Health and Nutrition Examination Survey (NHANES), the sensitivity of diagnosing retinopathy using one photograph taken with a nonmydriatic camera is an issue.

Proyecto VER (Vision Evaluation and Research), a population-based study of 4,774 residents of the Hispanic communities of Nogales and Tucson, Arizona, was designed in part to determine the prevalence rate of DR in the population with diabetes.

RESEARCH DESIGN AND METHODS

Selection of population

Proyecto VER is a population-based survey of noninstitutionalized Hispanics aged ≥40 years living in Pima and Santa Cruz counties in Arizona. Based on the 1990 census, random samples of block groups that contained at least 5% Hispanic residents aged ≥40 years in two strata (Nogales and Tucson) were selected. The probability of selection within the strata was proportional to the percentage of the Hispanic population aged ≥40 years. Every other household of the selected block groups in Nogales was listed and eligibility was determined. In Tucson, two-thirds of the households in selected block groups were listed; the change in listing procedures was due to substantial residential changes in Tucson since 1990, which resulted in fewer than

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Abbreviations: DR, diabetic retinopathy; NHANES, National Health and Nutrition Examination Survey; WESDR, Wisconsin Epidemiologic Study of Diabetic Retinopathy.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—*Comparison of selected characteristics in nonparticipants and participants*

Characteristics	Nonparticipant: no questionnaire or clinic exam‡	Nonparticipant: questionnaire only, no clinic examination*	Participant: questionnaire and clinic exam†
Age (years)			
40–49	180 (31)	385 (41)	1594 (33)
50–59	166 (29)	225 (24)	1362 (29)
60–69	105 (18)	165 (18)	984 (21)
70+	125 (22)	163 (18)	833 (18)
Sex			
Male	767 (52)	954 (42)	4774 (39)
Self report of diabetes (age-adjusted)	266 (11)	932 (17)	4757 (19)

Data are *n* (%). *A total of 17 people in this group did not report age, and one did not report sex; †17 people did not know whether they had received a diagnosis of diabetes; ‡of nonrespondents, 354 refused to answer questions regarding age, sex was not reported for 163, and 226 of 229 people responding to the short questionnaire answered the self-report of diabetes (although 69 did not report age, which would have enabled age adjustment).

expected eligible households in the selected block groups.

Procedures

Eligibility criteria for members in selected households included self-described Hispanics aged ≥40 years. After eligibility was determined, household members were recruited for interviews and clinical examinations at a central clinical site. Informed consent (in Spanish or English) was obtained following procedures approved by the Johns Hopkins Hospital Committee on Clinical Investigation. Eligible individuals who refused to participate were asked to respond to a short questionnaire, which included a question about the presence of diabetes.

The randomly selected block groups included 20,622 households, and 4,255 households (21%) had at least one eligible resident. From the 4,255 eligible households, 6,659 subjects were identified, 4,774 (72%) of whom completed the home questionnaire and the clinic visit. An additional 955 subjects (14%) completed the home questionnaire only, and 229 subjects (3%) refused the home questionnaire but completed the short form; the remaining 701 subjects (11%) refused to provide any information except for gender, Hispanic origin, and, in some cases, age.

Most home interviews (80%) were conducted in Spanish by trained bilingual interviewers. Questions included whether the diagnosis of diabetes had been confirmed by a physician and when the diagnosis had been made. Subjects responding affirmatively regarding physician diagnosis were also asked whether they were being treated with insulin, pills, diet, herbal remedies, or nothing.

At the clinic site, blood was drawn for the determination of HbA_{1c} level. All blood was stored in a refrigerator for no more than 5 days and shipped on ice to the reference lab (Dr. Michael Steffes, University of Minnesota). HbA_{1c} level was determined using high-performance liquid chromatography and standard controls, as described for the Diabetes Control and Complications Trial (12). Previous work in this laboratory has shown identical mean values in split samples and no assay drift over time (12).

Stereo fundus photographs of fields 1, 2, and 4 were taken through dilated pupils, using a Zeiss 30° fundus camera (Carl Zeiss, Oberkochen, Germany). These fields are as follows: center of the optic disc (field 1), center of the macula (field 2), and superior temporal to the macula (field 4). They were graded for the presence and severity of DR following a protocol developed by the Wisconsin Ocular Epidemiology Reading Center, Madison, Wisconsin. A preliminary and detailed grading was performed by one of the two graders, using the Wisconsin adaptation of the modified Airlie House classification of DR; discrepancies between the gradings were resolved by an edit by a senior grader, and if all three gradings were still discrepant, they were resolved by adjudication by a senior ophthalmologist (R.K.) (13,14).

Fundus photographs of at least one eye were obtained in 89% of subjects. Of the 11% of subjects for whom photographs were not obtained, the primary reasons were medical (contraindications to dilation), physical limitations (wheelchair-bound), refusal, and film lost in processing. No significant differences by gender or prior knowledge of diabetes status existed between those with and without photographs; however, older participants were less likely to have had photographs taken (data not shown). In 20 cases, DR could not be graded based on the photographs, primarily due to media opacity.

Blood pressure was measured according to a standardized protocol; three measurements of systolic and diastolic

Table 2—*Prevalence rate (per 100) of subjects with diabetes and questionable diabetes by age and sex*

	Age-groups (years)				
	40–49	50–59	60–69	70–79	80+
Men					
n	605	528	394	261	56
Diabetes	12.2	19.7	29.9	33.7	19.6
Questionable diabetes	1.0	1.3	3.3	2.7	5.4
Women					
n	936	830	588	373	140
Diabetes	11.8	23.2	29.9	34.6	25.0
Questionable diabetes	1.1	2.0	3.2	2.4	4.3
Population					
n	1,541	1,358	982	634	196
Diabetes	11.9	21.9	29.9	34.2	23.5
Questionable diabetes	1.1	1.8	3.3	2.5	4.6

Data are % unless otherwise indicated.

Table 3—*Prevalence rate (per 100) of retinopathy and macular edema, based on fundus photographs, by status of diabetes*

	Diabetes status		
DR signs*	Absent (subsample)	Questionable	Definitive
None†	82.5	79.0	52.0
Early changes‡	15.5	16.8	16.5
Moderate to severe, nonproliferative§	2.0	4.2	25.3
Proliferative‖	0	0	6.3
Macular Edema			
Not clinically significant	0.5	0	2.3
Clinically significant	0	1.0	5.1
n	200	95	918

*Diabetic retinopathy level could not be graded for 20 people; †WESDR grading system grades 10–13 (see text for further description); ‡WESDR grading system grades 14–20; §WESDR grading system grades 31–51; ‖WESDR grading system grades 60+.

pressure were taken, and an average of the second and third measurements were used (15). Hypertension was defined as *1*) a positive response to the question as to whether the patient had been told that he or she had hypertension and was currently under treatment for hypertension, *2*) systolic blood pressure ≥160 mmHg, or *3*) diastolic blood pressure ≥90 mmHg.

Definition of diabetes

Definite diabetes was defined as either an affirmative response to the question of whether diabetes had been diagnosed by a physician or having an HbA_{1c} of 7.0% or greater (16,17). Questionable diabetes was defined as those who reported no diagnosis of diabetes but who had HbA_{1c} values between 6.5 and 7.0%. All other subjects were classified as not having diabetes.

Definition of diabetic retinopathy

Photographs from all subjects with questionable and definite diabetes as well as a 5% random sample of individuals without diabetes were sent for masked grading. For these analyses, grades 10–13 were considered absence of DR, grades 14–20 were considered very early nonproliferative DR, grades 31–51 were considered moderate to severe nonproliferative DR, and grades 60 and higher were considered evidence of proliferative DR. Macular edema was graded separately. If at least one eye had evidence of DR, the subject was considered to have DR.

Statistical analyses

The prevalence rates of diabetes and DR are presented, stratified by age and gender. Differences in characteristics of participants and nonparticipants were assessed using χ^2 test or, when age-adjusted, Mantel Haenzel tests. After adjustment for age, subjects with self-reported diabetes were as likely to participate in the project as those who did not report diabetes.

The association of blood pressure or hypertension with early signs of DR in subjects without diabetes was assessed using logistic regression models, with adjustments for age and gender. Comparisons of our data with data from other studies were performed using the duration-specific rates from other studies and data supplied by Scot Moss and Dr. Ronald Klein from the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) cohort. For these comparisons, subjects with type 2 diabetes were defined as those not taking insulin or insulin users with onset of diabetes at ≥30 years of age. In addition, the study from San Antonio classified insulin users with onset ≥30 years of age who also had BMI ≥30 kg/cm^2 as having type 2 diabetes.

Duration of diabetes was calculated as time from year of diagnoses (as reported by the participant) to year of the examination at Proyecto VER.

RESULTS

— Differences in participation rates by age and gender were shown (Table 1). Men were less likely to participate, and the youngest and oldest individuals were also slightly less likely to complete both the home questionnaire and the clinic visit. Self-report of diabetes was no different between the participants and nonparticipants after age adjustment.

As expected, the distribution of values for HbA_{1c} in the total population was skewed (median value 5.9%). The values ranged from 3.0 to 16.6%; the 25th percentile value was 5.3%, and the 75th percentile value was 6.2%. Among the people with diabetes in this study, 15% were included based only on an HbA_{1c} value of 7% or higher ("newly diagnosed").

The prevalence rates of diabetes increased by age and were slightly higher in women (Table 2). The overall rate of diabetes in this population was 22%, increasing from 12% in subjects aged 40–49 years to 34% in subjects aged 70–79 years. Of our group of 1,044 individuals with diabetes, 21 (2.0%) were insulin users who had onset of diabetes before 30 years of age. The prevalence rate of questionable diabetes (defined as those who reported no diabetes but who had HbA_{1c} levels between 6.5 and 6.9%) did not increase consistently with age, and no gender differences were noted.

The prevalence rate of any DR in subjects with diabetes was 48%; 32% had moderate to severe nonproliferative or proliferative retinopathy (Table 3). Of the 5% subsample of subjects without diabetes for whom fundus photographs were obtained, the prevalence of very early DR-like changes was 15.5%, slightly lower than in subjects with diabetes or questionable diabetes. Subjects with diabetes had more severe changes than subjects with questionable or no diabetes. Clinically significant macular edema was present in 5.1% of the subjects with diabetes. No proliferative DR or clinically

Table 4—*Prevalence rate of very early retinopathy changes* by level of systolic and diastolic blood pressure in the 5% sample of people without diabetes*

Blood pressure	*n*	Percentage of retinopathy
Systolic blood pressure†		
<140	159	15.1
140–160	28	14.3
>160	9	33.3
Diastolic blood pressure†		
<90	172	15.1
90–100	16	18.8
>100	8	25.0
Total	196	15.8

Data are *n* and %. *Grades 14–20; †age- and sex-adjusted differences not significant ($P = 0.21$).

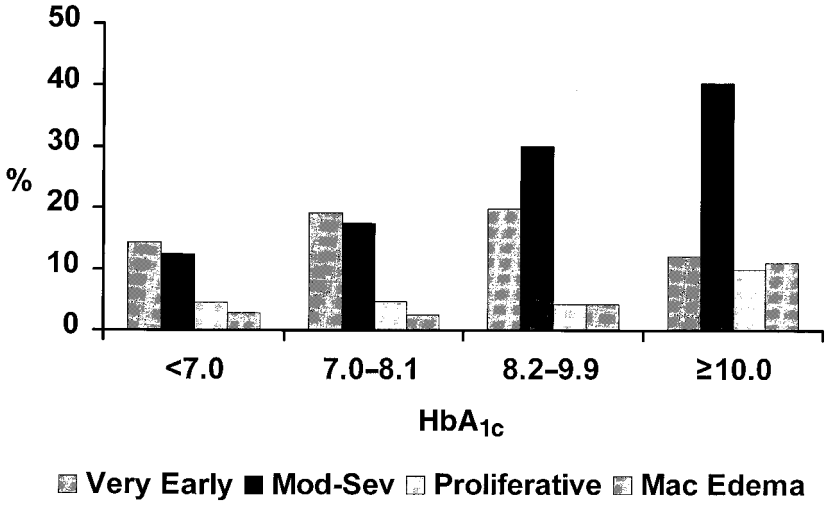

Figure 1—*HbA_{1c} levels and severity of retinopathy.*

significant macular edema was noted in subjects without diabetes.

The very early DR changes did not seem to be associated with increasing systolic or diastolic blood pressure or self-report of hypertension in this population (Table 4). Within the group of subjects who did not have diabetes, the prevalence rate of having very early DR-like changes seemed to increase with increasing diastolic or systolic blood pressure, but the test for trend was not significant, nor was Fisher's exact test. Blood pressure, adjusting for age and gender, was not associated with very early DR ($P = 0.21$ for systolic and diastolic blood pressure).

Among Hispanics with diabetes in this study, the severity of retinopathy increased with increasing level of HbA_{1c} (Fig. 1). The severity of retinopathy also increased with increasing reported duration of diabetes (Fig. 2); 9.3% of individuals with moderate to severe nonproliferative or proliferative retinopathy were newly diagnosed during the study. As discussed by others, the onset of diabetes in this group diagnosed during the study was probably 4–7 years earlier (18).

CONCLUSIONS — The prevalence rate of diabetes in the Mexican-Americans aged ≥40 years enrolled in Proyecto VER was high (estimated to be 22%). The rate of diabetes is similar to that reported by other studies in Mexican populations. In the Hispanic Health and Nutrition Examination survey, Flegal et al. reported a 23.9% prevalence rate of diabetes in Mexican-Americans aged 45–74 years, compared with 12% in non-Hispanic whites of the same age (2). In the San Antonio Heart Study, an estimated threefold difference in prevalence of type 2 diabetes in individuals aged ≥25 years was found between Mexican-Americans and non-Hispanic whites (8,19). Our findings that 15% were newly diagnosed by the project is identical to the 15% reported by Haffner et al. in their Hispanic population (9).

The duration-specific prevalence rates of DR we report herein for Hispanic individuals with diabetes were not different from data from the Wisconsin non-Hispanic white population (Table 5). These data are also consistent with reported findings from the San Antonio Heart Study Group (9) (Table 5). Although Haffner et al. reported higher rates in Hispanics than in whites (20), we are not able to replicate that finding. In part, the difference may be due to the inclusion of a BMI criterion by Haffner et al. for individuals with diabetes using insulin to be classified as having type 2 diabetes; this criterion was not used either in the WESDR data we presented nor in our current study. In addition, the other studies report data from the 1980s, whereas our study was conducted in 1997–1999; secular trends in prevalence rates of DR cannot be excluded, although our DR rates are similar to those of Haffner et al. in their 1979–1982 study (9).

Both our rates of DR and those of Haffner et al. are higher than those reported for the Mexican-Americans in the San Luis Valley diabetes study in Colorado (10). The rates in our study and those of the studies in Colorado, Texas, and Wisconsin all report higher rates than those reported from the NHANES. This discrepancy might be explained because the NHANES data are based on a single nonstereoscopic photograph taken through a nondilated pupil of a single eye. The likelihood of underascertainment of DR is higher using such an approach (21)

The prevalence of diabetes (and therefore the prevalence of DR) is sensitive to the definition of diabetes used in these studies. We did not use oral glucose tolerance testing or fasting plasma glucose concentration but instead relied on determination of HbA_{1c}. Our cutoff of 7% or

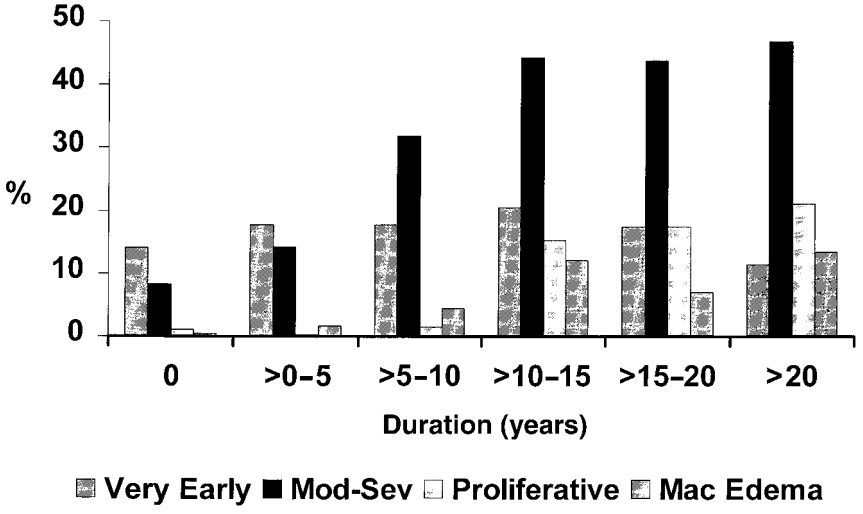

Figure 2—*Duration of diabetes and severity of retinopathy.*

Table 5—*Prevalence of diabetic retinopathy* among people with type 2 diabetes, by duration of diabetes*

Study site	Duration of diabetes (as reported)						
	Newly diagnosed	<5 years	5–9 years	5–14.9 years	≥15 years	<10 years	≥10 years
Proyecto VER Mexican-Americans (n = 907)							
Any DR	24	31	47	60	79	37	77
Moderate to severe DR	9	14	27	40	64	18	60
San Luis Valley Mexican-Americans (n = 187)							
Any DR	—†	20	—	49	60	—	—
Moderate to severe DR	—	—	—	—	—	—	—
San Antonio Mexican-Americans (n = 257)							
Any DR	16	35	46	—	86	39	85
Moderate to severe DR	4	—	—	—	—	16	66
NHANES III Mexican-Americans							
Any DR	—	14	—	41	54	—	—
Moderate to severe DR	—	—	—	—	—	—	—
WESDR Caucasians (n = 1,343)							
Any DR	—	32	45	53	79	39	76
Moderate to severe DR	—	12	27	33	64	19	59

Data are n. *Any DR is grade 14 and higher, and moderate to severe is grade 31 and higher; †data were not reported for this duration or level of severity.

higher has been shown to have maximum sensitivity and specificity compared with results of oral glucose tolerance tests, and it identifies individuals in need of pharmacologic intervention (16). Reported prevalences using this method are only slightly lower than with other methods (17), so our estimate of the prevalence of diabetes may be an underestimation. Others have suggested that elevated HbA_{1c} >6.5% but <7.0% may also represent elevated glucose levels requiring intervention by diet and/or exercise (16). We show our data separately for that group because there are few and no consistent age-related increases are shown. If we included that group in the definition of diabetes, our overall prevalence estimates would increase from 22 to 24%; both values are within the range reported by others for Hispanics in this age-group. Therefore, it is unlikely that our definition of diabetes is skewing our prevalence rates of DR either too high or too low.

We based the definition of DR on stereo fundus photographs of fields 1, 2, and 4 rather than photographs of all seven fields. This compromise was necessary to ensure a high response rate to our population-based study (in which photographs were obtained for all participants) while maintaining reasonable sensitivity for detecting DR. This choice may have resulted in some underascertainment of DR, with resulting lower prevalence estimates. However, the pattern of the association of DR we observed with duration of diabetes and level of HbA_{1c} is consistent with previous studies. In the San Antonio study, photographs of all seven fields were obtained of each eye in each subject with diabetes. Our duration-adjusted rates of DR matched the rates in this study most closely, even accounting for modest underascertainment of early noncentral lesions. In the San Luis Valley study, photographs of three fields were obtained through dilated pupils in all subjects with diabetes (similar to our protocol); however, our duration-adjusted rates were significantly higher. There is no good explanation at present for the lower rates in the San Luis Valley Study.

The rate of very early DR-like changes in subjects without diabetes or questionable diabetes was higher (15.5%) than has been reported in non-Hispanic white populations (5–10%) (22–24). The data in our population did not support a relationship between blood pressure or hypertension and signs of DR in those without diabetes. This is in contrast to the findings in the Caucasian populations of Wisconsin and Blue Mountain, Australia, in which an association was found (22,24). Photographs from all studies were read by the Wisconsin Reading Center. The Blue Mountain Study used a single measure of blood pressure, which could have misclassified the level of blood pressure, but such misclassification would have served to weaken any positive association. We followed a strict protocol for blood pressure ascertainment, in which three readings were obtained, and the average of the second and third values was used; this protocol is similar to that used in other studies of Mexican-Americans (25). If anything, our readings would have produced lower estimates of people with elevated blood pressure compared with some other studies. Thus, it seems unlikely that differences in ascertainment of blood pressure explain the lack of association observed. We did observe a nonsignificant trend of increasing prevalence rate of early retinopathy with increasing blood pressure, but the number of individuals in our subsample without diabetes may have been too small to detect a significant difference.

In summary, our study in a large population of Mexican-Americans confirms the high rate of diabetes and DR in this community. The finding that 15% of the cases of diabetes in this community were unknown before the survey and that, within this group, 23% of subjects had any retinopathy and 9% had moderate to severe retinopathy speaks to the special efforts that may be required to perform diabetes identification and control in this Hispanic population.

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