Is the Risk of Diabetic Retinopathy Greater in Non-Hispanic Blacks and Mexican Americans Than in Non-Hispanic Whites With Type 2 Diabetes?

A U.S. population study

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OBJECTIVE — To compare the risk for diabetic retinopathy in non-Hispanic white, non-Hispanic black, and Mexican-American adults with type 2 diabetes in the U.S. population.

RESEARCH DESIGN AND METHODS — Representative population-based samples of people aged ≥40 years in each of the three racial/ethnic groups were studied in the 1988–1994 Third National Health and Nutrition Examination Survey (NHANES III). Diagnosed diabetes was ascertained by medical history interview, and undiagnosed diabetes by measurement of fasting plasma glucose. A fundus photograph of a single eye was taken with a nonmydriatic camera, and a standardized protocol was used to grade diabetic retinopathy. Information on risk factors for retinopathy was obtained by interview and standard laboratory procedures.

RESULTS — Prevalence of any lesions of diabetic retinopathy in people with diagnosed diabetes was 46% higher in non-Hispanic blacks and 84% higher in Mexican Americans, compared with non-Hispanic whites. Blacks and Mexican Americans also had higher rates of moderate and severe retinopathy and higher levels of many putative risk factors for retinopathy. Blacks had lower retinopathy prevalence among those with undiagnosed diabetes. In logistic regression, retinopathy in people with diagnosed diabetes was associated only with measures of diabetes severity (duration of diabetes, HbA_{1c} level, treatment with insulin and oral agents) and systolic blood pressure. After adjustment for these factors, the risk of retinopathy in Mexican Americans was twice that of non-Hispanic whites, but non-Hispanic blacks were not at higher risk for retinopathy. These risks were similar when people with undiagnosed diabetes were included in the logistic regression models.

CONCLUSIONS — The prevalence and severity of diabetic retinopathy is greater in non-Hispanic blacks and Mexican Americans with type 2 diabetes in the U.S. population than in non-Hispanic whites. For blacks, this can be attributed to their higher levels of risk factors for retinopathy, but the excess risk in Mexican Americans is unexplained.

Diabetic retinopathy is one of the most frequent and serious complications of diabetes. Prevalence rates for retinopathy in people with type 2 diabetes have been reported from community-based studies (1–9). In two of these, comparisons were made between Hispanics and non-Hispanic whites, and conflicting results were obtained. In San Antonio, Texas (4), the risk of retinopathy (adjusted for statistically significant risk factors for retinopathy) was higher in Mexican Americans with previously diagnosed type 2 diabetes than in non-Hispanic whites (odds ratio 1.65). In San Luis Valley, Colorado (5), the multiple-adjusted relative risk was lower in Hispanics (odds ratio 0.40), which was confirmed by a prospective study (odds ratio 0.66) (10). In the one study comparing retinopathy in blacks and whites with type 2 diabetes, which involved patients who had not had a dilated eye examination in the past year, there was no statistically significant difference between these two groups in prevalence of retinopathy (9).

The Third National Health and Nutrition Examination Survey (NHANES III) provides an opportunity to reassess whether there are racial/ethnic differences in the risk of diabetic retinopathy. In NHANES III, we performed fundus photography in representative national samples of non-Hispanic white, non-Hispanic black, and Mexican-American adults who had been diagnosed with type 2 diabetes before the survey. Retinopathy was also measured in people who met fasting plasma glucose criteria for undiagnosed diabetes.

RESEARCH DESIGN AND METHODS

— NHANES III was conducted by the National Center for Health Statistics using a stratified multistage area probability design with oversampling of blacks and Mexican Americans (11). The response rate was 88%. There were 9,737 people aged ≥40 years who were interviewed for sociodemographic and medical history information and had a 4-h physical examination. Of these, 1,205 had been diagnosed with diabetes by a physician before the survey. Women who had diabetes diagnosed only during pregnancy were deleted from analysis (n = 18). Subjects with IDDM, identified as those with age at diagnosis <30 years who had continuous or almost continuous insulin use

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Abbreviations: NHANES III, Third National Health and Nutrition Examination Survey.

since diagnosis of diabetes, were also deleted from analysis (n = 7). The remaining 1,180 subjects were considered to have type 2 diabetes.

Gradable fundus photographs were obtained for 939 subjects with type 2 diabetes (80%), including 345 non-Hispanic whites, 261 non-Hispanic blacks, 308 Mexican Americans, and 25 subjects of other race/ethnicity. Reasons for not having a gradable photograph included problems with the camera or film, insufficient time to complete the examination, and problems with the eye, such as insufficient pupil dilation, lens opacity, eye movement, or corneal change (n = 187) or having a fundus photograph that was not gradable (n = 54). There were no statistically significant differences in a variety of variables related to retinopathy between subjects with gradable photographs and subjects without gradable photographs.

The 8,550 subjects without diagnosed diabetes were divided into two half-samples. The subjects in one half-sample were asked to fast overnight for at least 9 h for a morning examination; those in the other half-sample were asked to fast for at least 4 h for an afternoon examination. Plasma glucose after a fast of the requested length of time was obtained for 7,617 subjects, and gradable fundus photographs were obtained for 6,588 of these. American Diabetes Association criteria (12) were used to define subjects with undiagnosed diabetes (fasting plasma glucose ≥126 mg/dl, n = 288). Prevalence of undiagnosed diabetes was computed after weighting the data by age, sex, and race and adjusting for the absence of people with diagnosed diabetes in the two half-samples. The ratio of diagnosed to undiagnosed diabetes was ~2:1, as previously described (13). Prevalence of retinopathy and distribution of HbA_{1c} were similar for the morning and afternoon half-samples. Consequently, these two half-samples were combined in the analysis.

In the fundus photograph procedure, a nonstereoscopic color 45° photograph centered between the optic nerve and the macula was taken of one randomly selected eye (11). The camera was a Canon CR4-45NM nonmydriatic fundus camera incorporating an infrared video camera to allow photographs to be taken in the darkened examination room without the use of dilating drops. The photographs were graded by masked photograders at the University of Wisconsin Department of Ophthalmology under the direction of one of us (R.K.), using a modification of the Airlie House classification system (14–16). Quality of grading was evaluated through regrading a sample of photographs by the same grader, a second grader, and an ophthalmologist. For lesions typical of diabetic retinopathy, agreement between pairs of regraders was 95–97%, and κ ranged from 0.72 to 0.86, indicating excellent agreement. Some sample individuals had the same eye photographed twice to assess comparability of grading; κ for the retinopathy scores for these pairs was 0.82.

HbA_{1c} was measured at the University of Missouri, Columbia, by a high-performance liquid chromatographic assay, as used in the Diabetes Control and Complications Trial (17). Serum total cholesterol was measured enzymatically in the Johns Hopkins University Lipid Research Clinic, Baltimore, MD, using a commercially available reagent mixture (18). Blood pressure was measured with subjects in the sitting position, using a standard mercury sphygmomanometer; the mean of three blood pressure measurements was used.

Statistical analyses were conducted using SAS (19) and SUDAAN (20), a statistical software package that adjusts for the cluster sample design of the survey in computing variance estimates. Data were weighted to correct for the oversampling of Mexican Americans and non-Hispanic blacks. Multiple logistic regression was conducted by a backwards stepwise procedure. Because of the inherent relationships among age, duration of diabetes, and age at diagnosis of diabetes, these variables could not be entered in the same model. When diabetes duration was present in the model, neither age nor age at diabetes diagnosis was statistically significant. Throughout the model reduction process, the odds ratios for retinopathy in Mexican Americans and non-Hispanic blacks were stable, indicating that the effect of race/ethnicity was not influenced by other variables in the model. Interactions of race/ethnicity and the significant predictor variables were entered into the final model, but none were statistically significant.

Table 1—*Prevalence of diabetic retinopathy in U.S. adults aged ≥40 years, NHANES III, 1988–1994*

	Non-Hispanic white	Non-Hispanic black	Mexican-American
Diagnosed diabetes			
Any retinopathy	18.2 (12.9–23.6)	26.5 (19.3–33.6)	33.4 (26.7–40.1)
Mild nonproliferative retinopathy	12.3 (9.7–14.8)	15.5 (10.2–20.8)	15.4 (9.3–21.6)
Moderate retinopathy	5.2 (3.1–7.2)	9.2 (4.7–13.7)	12.4 (6.0–18.8)
Proliferative retinopathy	0.9 (0–1.7)	1.8 (0.5–3.0)	5.6 (3.1–8.0)
Undiagnosed diabetes			
Any retinopathy	7.7 (1.5–13.8)	1.5 (0–3.6)	9.9 (2.0–17.7)

Data are % (95% CI). Diagnosed diabetes: any retinopathy, P = 0.07 for non-Hispanic whites vs. non-Hispanic blacks, $P < 0.01$ for non-Hispanic whites vs. Mexican Americans, P = 0.14 for non-Hispanic blacks vs. Mexican Americans; mild retinopathy, P = NS for all comparisons; moderate retinopathy, $P < 0.05$ for non-Hispanic whites vs. non-Hispanic blacks, $P < 0.01$ for non-Hispanic whites vs. Mexican Americans, P = NS for non-Hispanic blacks vs. Mexican Americans; proliferative retinopathy, P = NS for non-Hispanic whites vs. non-Hispanic blacks, $P < 0.05$ for Mexican Americans vs. non-Hispanic whites and vs. non-Hispanic blacks. Undiagnosed diabetes: P = 0.07 for non-Hispanic whites vs. non-Hispanic blacks, P = 0.05 for non-Hispanic blacks vs. Mexican Americans, P = NS for non-Hispanic blacks vs. Mexican Americans.

RESULTS — Table 1 shows prevalence of diabetic retinopathy in the three racial/ethnic groups. Prevalence of any lesions of retinopathy in those with diagnosed diabetes was 46% higher in non-Hispanic blacks (P = 0.07) and 84% higher in Mexican Americans ($P < 0.01$) than in non-Hispanic whites. Prevalence of more severe levels of retinopathy was also greater in non-Hispanic blacks and Mexican Americans. Within each racial/ethnic group, differences in retinopathy prevalence by age and sex were not statistically significant. Prevalence of retinopathy among those with undiagnosed diabetes was lower for non-Hispanic blacks than non-Hispanic whites (P = 0.07) and Mexican Americans (P = 0.05) (Table 1).

The prevalence of retinopathy in those with diagnosed diabetes increased from 11.8% at <5 years since diagnosis of diabetes to 36.0% at ≥15 years since diagnosis ($P < 0.001$). There were no significant differences among the three racial/ethnic groups in retinopathy prevalence at <5 years' duration of diabetes. However, at

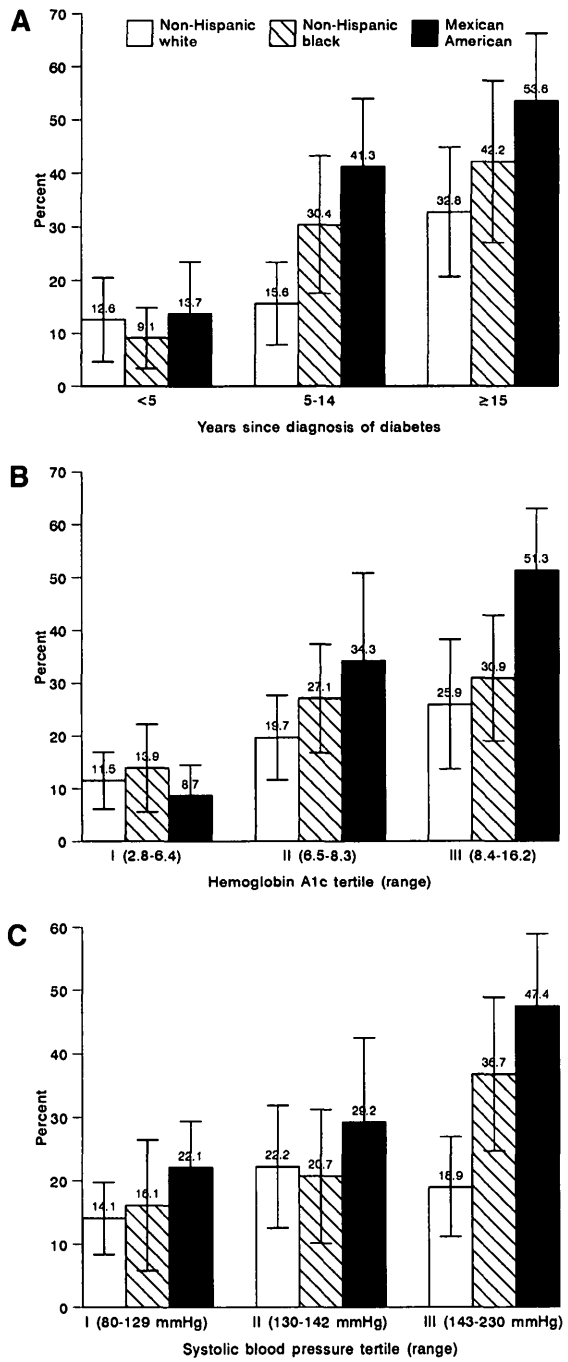

Figure 1—*Prevalence of diabetic retinopathy in adults aged ≥40 years with diagnosed type 2 diabetes, by duration of diabetes, HbA_{1c}, systolic blood pressure, and race/ethnicity, NHANES III, 1988–1994. A: Trend of increasing retinopathy prevalence with longer duration of diabetes, P < 0.01 in all three racial/ethnic groups. P > 0.4 for racial/ethnic comparisons at diabetes duration <5 years; P < 0.05 for non-Hispanic whites vs. non-Hispanic blacks and vs. Mexican Americans at 5–14 years; P < 0.05 for non-Hispanic whites vs. Mexican Americans at ≥15 years. B: Trend of increasing retinopathy prevalence with higher HbA_{1c} level, P = 0.06 for non-Hispanic whites, P = 0.02 for non-Hispanic blacks, and P < 0.001 for Mexican Americans. P > 0.3 for all racial/ethnic comparisons at HbA_{1c} 2.8–6.4; P > 0.2 for all racial/ethnic comparisons at HbA_{1c} 6.5–8.3; P = 0.5 for non-Hispanic whites vs. non-Hispanic blacks, P = 0.006 for non-Hispanic whites vs. Mexican Americans, and P = 0.02 for non-Hispanic blacks vs. Mexican Americans at HbA_{1c} 8.4–16.2. C: Trend of increasing retinopathy prevalence with higher systolic blood pressure, P = 0.15 for non-Hispanic whites, P < 0.05 for non-Hispanic blacks and Mexican Americans. P > 0.2 for racial/ethnic comparisons at 80–129 mmHg and 130–142 mmHg; P < 0.05 for non-Hispanic blacks and Mexican Americans vs. non-Hispanic whites at systolic blood pressure 143–230 mmHg.*

5–14 years and at ≥15 years, Mexican Americans had the highest rate of diabetic retinopathy, and non-Hispanic whites had the lowest rate ($P < 0.05$) (Fig. 1).

Retinopathy was more frequent as HbA_{1c} level increased, rising from 11.3% in the lowest tertile of HbA_{1c} to 28.0% in the highest tertile ($P < 0.001$). Rates of retinopathy were similar among the three groups in the lowest tertile, but in the second and third tertiles of HbA_{1c}, the rate was highest for Mexican Americans ($P = 0.02$) (Fig. 1). The rate of retinopathy rose from 14.0% in the first tertile of systolic blood pressure to 25.0% in the third tertile. Retinopathy prevalence in the third tertile was higher for non-Hispanic blacks and Mexican Americans than non-Hispanic whites ($P < 0.05$) (Fig. 1).

Table 2 presents a summary of putative risk factors for diabetic retinopathy. Non-Hispanic blacks and Mexican Americans had higher levels of many of these risk factors, such as less education, earlier age at diagnosis, longer duration since diabetes diagnosis (blacks), higher proportions using insulin (blacks) or oral agents (Mexican Americans), larger proportions in the higher tertiles of HbA_{1c} and systolic blood pressure, and larger proportions who smoked cigarettes (blacks).

Table 3 shows the results of logistic regression models to evaluate the independent effects of these variables on the risk of retinopathy. The risk was significantly associated only with measures of diabetes severity (duration of diabetes, HbA_{1c}, insulin use, oral agent use). There was a modest effect of systolic blood pressure that was marginally nonsignificant. After adjustment for these factors in the regression models, non-Hispanic blacks were not at higher risk for diabetic retinopathy than non-Hispanic whites, but Mexican Americans were twice as likely to have retinopathy as non-Hispanic whites.

In the model, the risk of retinopathy increased with longer duration of diabetes, higher HbA_{1c} level, and higher systolic blood pressure. Treatment with insulin and oral agents was associated with increased risk, but when both of these variables were included in the model, HbA_{1c} was not statistically significant because of colinearity with these diabetes therapy variables (Table 3). The risk of retinopathy was not associated with age or age at diabetes diagnosis (when diabetes duration was present in the model), sex, education, cigarette smoking, serum total cholesterol, or diastolic blood pressure ($P > 0.2$). Throughout the model

Table 2—*Distribution of potential risk factors for diabetic retinopathy in adults aged ≥40 years with previously diagnosed type 2 diabetes*

	Non-Hispanic white	Non-Hispanic black	Mexican-American
Mean age (years)	62.5	60.3	57.4
Male (%)	49.2	34.7	40.3
High school education or greater (%)	63.4	42.0	25.7
Mean age at diabetes diagnosis (years)	53.2	49.8	48.0
Distribution by years since diabetes diagnosis (%)			
<5	38.7	32.6	40.9
5–14	38.1	38.7	34.5
≥15	23.2	28.7	24.6
Distribution by diabetes treatment (%)			
Insulin	23.8	42.7	20.8
Oral agents	48.9	35.9	55.4
No pharmacologic therapy	27.3	21.4	23.8
Distribution by HbA_{1c} tertile (%)			
Tertile 1 (2.8–6.4)	35.6	27.6	28.4
Tertile 2 (6.5–8.3)	34.3	35.2	36.5
Tertile 3 (8.4–16.2)	30.0	37.1	35.2
Distribution by systolic blood pressure tertile (%)			
Tertile 1 (80–129 mmHg)	36.1	31.6	37.8
Tertile 2 (130–142 mmHg)	32.4	26.1	25.7
Tertile 3 (143–230 mmHg)	31.5	42.4	36.4
Current cigarette smoking (%)	14.3	25.7	15.9
Mean diastolic blood pressure (mmHg)	74.6	76.7	76.8
Mean pulse pressure (mmHg)	61.8	63.9	62.8
Mean arterial pressure (mmHg)	95.2	98.0	97.7
Mean serum total cholesterol (mg/dl)	225.1	222.1	220.2

Data are for subjects with gradable fundus photographs.

reduction process, the odds ratios for retinopathy in Mexican Americans and non-Hispanic blacks were stable, indicating that the effect of race/ethnicity was not influenced by other variables in the model. Interactions of race/ethnicity and the significant predictor variables were entered into the final models, but none were statistically significant. This indicates, for example, that insulin had the same effect on the risk of retinopathy in all three racial groups.

Retinopathy prevalence for those with undiagnosed diabetes is shown in Table 1. Mean HbA_{1c} differed by racial/ethnic group and was 6.7% (6.3–7.0) for non-Hispanic whites, 8.2% (7.0–9.4) for non-Hispanic blacks, and 7.8% (7.0–8.5) for Mexican Americans with undiagnosed diabetes. Table 4 shows logistic regression models that include both diagnosed and undiagnosed type 2 diabetes and adjust for these differences in HbA_{1c} levels. As in the regression models for diagnosed diabetes (Table 3), the risk of retinopathy for Mexican Americans was twice that of non-Hispanic whites, and the risk for non-Hispanic

Table 3—*Multiple logistic regression analysis of risk factors for diabetic retinopathy in subjects aged ≥40 years with previously diagnosed type 2 diabetes*

	Model without diabetes therapy		Model with diabetes therapy	
	Odds ratio (95% CI)	*P*	Odds ratio (95% CI)	*P*
Race/ethnicity (vs. non-Hispanic white)				
Mexican-American	1.93 (1.10–3.40)	0.023	2.15 (1.15–4.04)	0.018
Non-Hispanic black	1.15 (0.65–2.04)	0.617	0.94 (0.54–1.66)	0.841
Duration of diabetes (per 10 years since diagnosis)	1.67 (1.27–2.19)	0.0005	1.60 (1.26–2.03)	0.0004
HbA_{1c} (per 1-U increase)	1.23 (1.07–1.42)	0.006	1.10 (0.96–1.28)	0.184*
Systolic blood pressure (per 10-mmHg increase)	1.11 (0.99–1.25)	0.091	1.11 (1.00–1.24)	0.065
Diabetes therapy (vs. diet-treated)				
Insulin			10.05 (3.78–26.75)	0.0000
Oral agents			4.07 (1.75–9.45)	0.0016

*When both insulin and oral agents were included in the regression model, the odds ratio for HbA_{1c} was not statistically significant because of colinearity among these variables. Other variables tested in logistic regression models that were not statistically significant ($P > 0.20$) were age and age at diabetes diagnosis (nonsignificant in models that included duration of diabetes), sex, years of education, cigarette smoking, serum total cholesterol, diastolic blood pressure, mean arterial pressure, squared terms for all continuous variables (to examine whether there were nonlinear relationships), and interactions of the racial/ethnic variables non-Hispanic black and Mexican American with the statistically significant variables (to examine whether any subgroup was at higher risk for retinopathy, such as Mexican Americans who take insulin).

Table 4—*Multiple logistic regression analysis of risk factors for diabetic retinopathy in subjects aged ≥40 years with previously diagnosed or undiagnosed type 2 diabetes*

	Model without diabetes therapy		Model with diabetes therapy	
	Odds ratio (95% CI)	*P*	Odds ratio (95% CI)	*P*
Race/ethnicity (vs. non-Hispanic white)				
Mexican-American	1.84 (1.07–3.14	0.027	1.99 (1.10–3.60	0.024
Non-Hispanic black	1.04 (0.61–1.77	0.874	0.86 (0.50–1.47	0.575
Duration of diabetes (vs. undiagnosed diabetes)				
≥10 years	4.32 (1.96–9.51	0.0005	0.97 (0.28–3.32	0.958
<10 years	1.68 (0.98–2.88	0.057	0.43 (0.15–1.18	0.101
HbA_{1c} (per 1-U increase)	1.18 (1.05–1.32	0.006	1.08 (0.96–1.21	0.232*
Systolic blood pressure (per 10-mmHg increase)	1.11 (0.96–1.28	0.164	1.11 (0.98–1.25	0.119
Therapy (vs. diet-treated and undiagnosed diabetes)				
Insulin			10.01 (3.72–26.91	0.0000
Oral agents			3.75 (1.67–8.40	0.002

*When both insulin and oral agents were included in the regression model, the odds ratio for HbA_{1c} was not statistically significant because of colinearity among these variables.

blacks was not significantly different from that of non-Hispanic whites.

CONCLUSIONS — The NHANES III survey provides information on diabetic retinopathy in nationwide population-based samples of adults with type 2 diabetes in three racial/ethnic groups. Standardized procedures were used to obtain color fundus photographs, and an objective masked grading system was used to evaluate these photographs for diabetic retinopathy. We found higher rates of retinopathy in non-Hispanic blacks and Mexican Americans compared with non-Hispanic whites. The higher risk remained in Mexican Americans, but not in non-Hispanic blacks, after adjusting for the severity of diabetes (diabetes duration, HbA_{1c} level, insulin and oral agent use) and systolic blood pressure.

The higher risk in Mexican Americans in NHANES III is concordant with the cross-sectional findings from San Antonio, Texas, but is discordant with the cross-sectional and prospective findings from San Luis Valley, Colorado. No immediate reason for this discrepancy is apparent. All three studies were controlled in a similar fashion for differences in diabetes severity, duration, glycemic control, and blood pressure between Mexican Americans and non-Hispanic whites. The significant predictors of retinopathy in multiple logistic regression and the magnitude of their effects are similar in the three studies, except for the lower odds ratio associated with Mexican-American ethnicity in the San Luis Valley.

What unmeasured variables might account for the difference among the studies? It is possible that medical care and glycemic control before the studies were better in non-Hispanic whites than in Mexican Americans in San Antonio and NHANES III but were poorer in non-Hispanic whites than Mexican Americans in the San Luis Valley. However, this has been discounted as an explanation for the racial/ethnic differences (4,5,10). In the NHANES III logistic regression models, we controlled for glycemia levels in those with diagnosed and undiagnosed diabetes, and the higher risk of retinopathy in Mexican Americans remained. There were no statistically significant interactions of race/ethnicity with the diabetes severity variables or systolic blood pressure in logistic regression in NHANES III. This indicates that the effect of the risk factors is similar in all three racial/ethnic groups and that there is no differential effect that might explain the higher risk of retinopathy in Mexican Americans. An explanation may be found in genetic factors, which are important in the incidence of diabetic microvascular disease (21–23). Such genetic studies, if conducted in various racial/ethnic groups, may be fruitful in explaining the differential susceptibility to diabetic retinopathy.

In NHANES III, the adjusted odds ratio for risk of retinopathy in non-Hispanic blacks relative to non-Hispanic whites is close to unity (Tables 3 and 4). Nevertheless, the prevalence of retinopathy is higher in non-Hispanic blacks. This appears to be due to a higher frequency of risk factors for retinopathy in this group. For example, 37.1% of non-Hispanic blacks are in the upper tertile of HbA_{1c}, and 42.4% are in the upper tertile of systolic blood pressure, compared with 30.0 and 31.5%, respectively, of non-Hispanic whites. The proportion treated with insulin is also substantially higher (43 vs. 24%), and diabetes duration is longer (11 vs. 9 years). For Mexican Americans, higher levels of risk factors can explain only part of their excess risk of retinopathy, since the odds ratio for Mexican-American ethnicity from logistic regression was ~2.

In summary, the nonsignificant risk from logistic regression for diabetic retinopathy in non-Hispanic blacks relative to non-Hispanic whites and the significant risk in Mexican Americans suggests that diabetes severity and glycemic control may explain the black/white differences but not the Mexican-American/white differences. Other reasons for the higher risk in Mexican Americans need to be sought.

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