Incidence and Progression of Diabetic Retinopathy in Hispanics and Non-Hispanic Whites With Type 2 Diabetes

San Luis Valley Diabetes Study, Colorado

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OBJECTIVE — To learn if Hispanic people with type 2 diabetes have excess incidence and/or progression of diabetic retinopathy and to explore the association of risk factors with diabetic retinopathy.

RESEARCH DESIGN AND METHODS — There were 244 subjects with type 2 diabetes (65.3% Hispanic) with at least one follow-up visit between 1984 and 1992 examined for the development of retinopathy over a median of 4.8 years (range 2.0–6.6 years). Stereo fundus photos were graded by the University of Wisconsin Reading Center.

RESULTS — Of the 169 subjects without retinopathy at baseline, 47 developed some retinopathy, an incidence rate of 63.7 per 1,000 person-years (PY), or a 4-year cumulative incidence of 22.5%. The Hispanic incidence rate was 58.3/1,000 PY (95% CI: 39.4–83.3), which was lower than among non-Hispanic whites, 76.1/1,000 PY (44.3–121.9). Progression occurred in 24 of the 75 subjects with retinopathy at baseline, a 4-year cumulative rate of 24.1%. Logistic regression showed that insulin treatment was associated with higher risk of any retinopathy (odds ratio [OR] = 8.45, 2.65–26.97), and both systolic blood pressure (odds ratio [OR] = 1.58, 0.99–2.52) and total GHb (OR = 1.46, 0.99–2.17) nearly attained statistical significance. After adjustment for multiple potential risk factors, the Hispanic/non-Hispanic white OR was 0.66 (0.28–1.57).

CONCLUSIONS — No excess risk for incident retinopathy was found among Hispanic compared with non-Hispanic white subjects in this population. These results are consistent with our previously reported prevalence data from the same population but differ from reports of excess prevalence among Texas Hispanics. No other Hispanic incidence data are available to assist in reconciling this difference.

Diabetic retinopathy has been recognized for several decades as one of the most prevalent complications of both non-insulin-dependent (type 2) and insulin-dependent (type 1) diabetes (1–4). With increases in the numbers of people with diabetes, retinopathy has become one of the foremost causes of new cases of blindness and vision loss in adults in the United States (1,3). Study of the incidence and progression of diabetic retinopathy and associated risk factors is important in the prevention of its development and of the visual impairment caused by this complication.

Hispanics are known to have a two- to fourfold increased risk of type 2 diabetes compared with non-Hispanic whites (NHW) (5), but data comparing retinopathy prevalence have been contradictory (4–6). Excess prevalence of retinopathy was noted in San Antonio Mexican-Americans (6), but a significant though small deficit among Hispanics compared with NHW subjects was seen in our previous prevalence study (4). No incidence data for diabetic retinopathy in these populations has been published. In the present study, the incidence and progression of diabetic retinopathy were examined to learn whether Hispanics had excess risk compared with NHWs with type 2 diabetes living in the San Luis Valley of Colorado. Because glucose control, hypertension, type of therapy, and diabetes duration, among other risk factors, are associated with diabetic retinopathy (1,4,6–20), we also examined these and other factors to see if they accounted for altered Hispanic-to-NHW incidence rates.

RESEARCH DESIGN AND METHODS

Population

The San Luis Valley Diabetes Study was undertaken to examine the prevalence and incidence of type 2 diabetes and to study risk factors for the development of type 2 diabetes and its complications. Methods and more details of the study design have been described in previous publications (4,21). People with diabetes were identified in three ways: *1*) medical record review and community publicity identified people with prevalent diabetes ("known diabetes") during the baseline period from 1984–1986; 2) all community incident cases were identified from medical practices using active surveillance from 1986–1988; and 3) a stratified sample of 1,351 people not known to have diabetes was screened for diabetes using an oral glucose tolerance test, and 71 people were found to have diabetes. Of the 1,791 people who attended a baseline clinic visit, 430 (24%) were confirmed to have type 2 diabetes by World Health Organization criteria (22) or use of insulin

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Abbreviations: HR, hazard ratio; NHW, non-Hispanic white; OR, odds ratio; PY, person-years; WESDR, Wisconsin Epidemiologic Study of Diabetic Retinopathy.

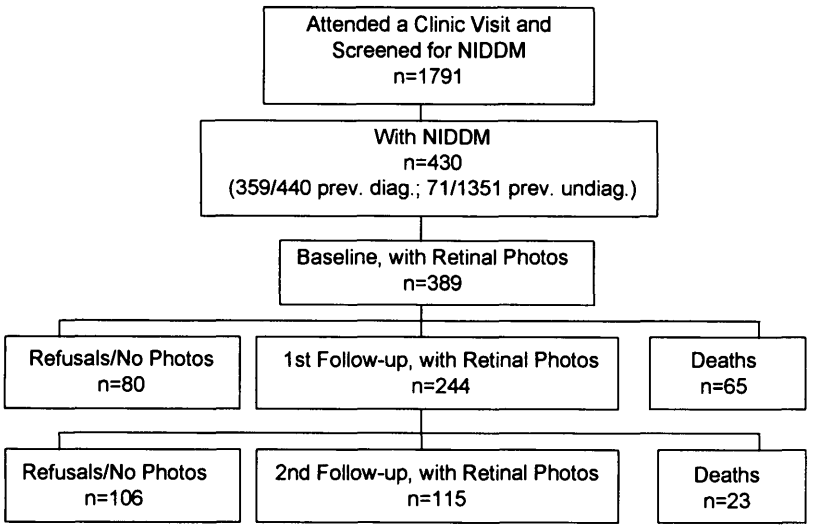

Figure 1—*Participation in follow-up for retinopathy assessment in the San Luis Valley Diabetes Study, 1984–1992.*

or oral agents. Subjects were classified as having type 1 diabetes if C-peptide levels were <0.1 pmol/ml or lacking C-peptide levels, age at onset was <18 years, and insulin treatment was for not less than all but 1 year of duration (21). Subjects with type 1 diabetes were removed from the study. Study subjects were Hispanic and NHW people, aged 20–74 years, who were current residents of Alamosa or Conejos counties in southern Colorado, who had type 2 diabetes at the baseline visit, and who spoke either English or Spanish.

The baseline visits occurred between May 1984 and August 1988. Of the total group screened, 430 people were identified with type 2 diabetes, and 389 subjects (172 men and 217 women) had retinal photographs at the baseline visit (90.5%) (Fig. 1). At the first follow-up visit an average of 4.8 years later (SD = 1.4, range 2.0–6.6), 252 subjects returned (64.8%). Of these people, 244 (96.8%) had gradable retinal photographs. Among the 145 people not returning, 65 had died (44.8%), 67 refused (46.1%), and 5 became ineligible due to terminal illness or inability to physically be transported to the clinic site (3.5%). Additionally, four subjects did not have photos taken, and four subjects had ungradable photos (5.6%). One hundred forty-three subjects completed a second follow-up visit an average of 5.4 years after baseline (58.6%), with a range of follow-up time from 3.9 to 6.5 years. Of these, 115 had gradable photographs (80.4%); 5 subjects had no photos at either visit (3.5%). Of the people not returning, 23 had died (21.7%) and 83 refused (78.3%). Analyses presented here were restricted to those subjects identified with type 2 diabetes at the baseline visit, 1984–1988, and who had one or more follow-up visits with retinal photographs (n = 244) between 1988 and 1992.

Retinopathy classification

After pharmacological dilation of pupils, stereoscopic fundus photographs were taken of Diabetic Retinopathy Study fields I, II, and IV (23,24). These photographs were graded at the University of Wisconsin Fundus Photography Reading Center using the modified Airlie House Classification scheme (24). A summary classification scheme was used for assigning severity of retinopathy as the worst eye for each patient (Table 1) (4,25,26). The distribution of baseline retinopathy prevalence for all subjects seen at baseline (n = 389) and those in this report with follow-up (n = 244) are also shown in Table 1.

The incidence of any new retinopathy was estimated for all those who had no retinopathy at baseline examination (n = 169) and who had at least one follow-up examination. Incidence and progression were defined as an increase in the retinopathy severity grade of two steps or more at either of the follow-up examinations. Regression, or improvement, of retinopathy was defined as a two-step or more decrease in the severity of retinopathy at the follow-up exam(s) in those subjects positive for any retinopathy at baseline (n = 75).

Table 1—*Classification scheme for retinopathy severity and numbers of subjects by baseline severity category, San Luis Valley Diabetes Study, 1984–1992*

Grade	Definition	All subjects at baseline (n = 389)	Subjects with follow-up photos (n = 244)
10, 12	Normal fundus, or abnormal fundus not characteristic of DR	250 (64.3)	169 (69.3)
15	Background DR with no MA but ≥1 of the following: hemorrhage, soft exudates, or IRMA	11 (2.8)	7 (2.9)
20	Background DR with MA only	42 (10.8)	27 (11.1)
30	Background DR with MA and >1 of the following: hemorrhage and MA < standard photo 2A,* <3 hard exudates, venous looping, questionable soft exudates, questionable IRMA, and questionable venous beading	30 (7.7)	21 (8.6)
40	Preproliferative DR with MA and ≥1 of the following: hemorrhage and MA >2A,* <3 hard exudates, soft exudates, IRMA, and venous beading	39 (10.0)	18 (7.4)
60	Proliferative DR with fibrous proliferations but without new vessels	1 (0.3)	0 (0.0)
65	Proliferative DR with ≥1 of the following: new vessels elsewhere, new vessel disk <10A,* preretinal hemorrhage, and vitreous hemorrhage	13 (3.3)	2 (0.8)
70	Proliferative DR, high-risk characteristics	3 (0.8)	0 (0.0)

Data are n (%). DR, diabetic retinopathy; MA, microaneurysms; IRMA, intraretinal microvascular abnormality. *For definition, see references 25 and 26.

Risk factors

Subjects were interviewed by a bilingual interviewer masked to retinopathy status and examined by a trained nurse clinician. Ethnicity was defined by response to the question "Are you of Spanish or Hispanic origin or descent" from the 1980 U.S. Census (27). Family history of diabetes was positive if the subject reported that a parent or sibling had been diagnosed with diabetes. Subjects were classified as current, former, or never smokers at the time of each clinic visit based on a self-report. Those subjects who had smoked <100 cigarettes in their lifetime were considered to have never smoked. BMI was calculated as current weight (kg) divided by height (m^2) in a scrub suit. Glycemia was assessed by the percentage of glycosylated hemoglobin (total GHb) present, determined by a microcolumn method (ion-exchange chromatography; Quik-Sep Fast Hemoglobin Test System, Isolab, Akron, OH) at the baseline examination. Total GHb was measured at the follow-up visits using a finger-stick collection on filter paper that was mailed to the laboratory of Dr. David Goldstein, University of Missouri, for assay by affinity chromatography. Overall correlation between these two methods was $r = 0.89$, and the regression relationship was as follows: filter paper value = 1.8 + 0.8 (venous ion-exchange chromatography value) (28). The data from this second method, adjusted using the regression equation above, were used in Cox proportional hazards analysis, which incorporated follow-up data. Duration of diabetes was by self-report. Systolic and diastolic blood pressures were measured as the average of the last two of three fifth-phase supine measurements with a mercury sphygmomanometer. Hypertension was defined as having blood pressure >140 mmHg systolic and/or 90mmHg diastolic, or being on antihypertensive medication (29). Kidney function was assessed by total urine protein-to-creatinine ratio (30). Serum triglyceride levels were measured using an enzymatic procedure (31). Fasting serum cholesterol was measured by the esterase-oxidase method (32), and total HDL cholesterol was determined enzymatically following dextran sulfate magnesium precipitation (33).

Statistical analysis

Incidence density calculations using person-years were completed for the entire group in follow-up and by ethnicity by accumulating all follow-up time until the last visit or an endpoint developed. Significance testing for these rates was assessed using an exact binomial test (PEPI computer program, Rates2 [34]). Cumulative incidence rates were calculated from these incidence density values using the equation $CI_t = 1 - e^{-I\Delta t}$ (35), where CI is the cumulative incidence, t is time, and I is incidence density, for a 4-year period of follow-up to be comparable to those of Klein et al. (12).

All data were analyzed using Statistical Analysis Systems (SAS) statistical package software (SAS Institute, Cary, NC, Version 6 for Windows). Multiple logistic regression was used to assess the independent effect of potential risk factors.

Model fitting was accomplished in several steps. Initially a full model was fitted that included the independent variables sex, ethnicity, clinical age (assessed in 10-year increments), duration of type 2 diabetes (assessed in 5-year increments), diabetes treatment (insulin, oral agents, or none), systolic blood pressure, diastolic blood pressure, urine protein-to-creatinine ratio, serum triglyceride, total cholesterol, total HDL, family history of diabetes, and BMI. Time since a baseline visit was included in the models to account for differential follow-up time. Akaike's information criteria (36) was used as an indicator of model fit. Previous research has implicated potential interaction of ethnicity with smoking, ethnicity with type of diabetes treatment, and smoking with diabetes treatment (4,12) on retinopathy. These were assessed in the analyses and removed from the model one by one, starting with the term with the highest P value, and the effect on the -2 log likelihood as a measure of model fit was noted. None of the interaction terms were retained in later models due to lack of significance or inconsistent patterns in subgroups with small numbers. Next, main effects variables were removed individually, and the effect of their removal on the association between ethnicity and the dependent variable, retinopathy status, was noted. Age, sex, and ethnicity were retained in all models. In the multivariate models, time was not significantly related to the outcome. Inclusion of time did not alter the association between ethnicity and retinopathy. Development of retinopathy was also evaluated using Cox proportional hazards regression (Proc PHREG, Discrete ties) in SAS statistical software (SAS Institute, Version 6 for Windows), and the generally similar results are discussed in text only.

Table 2—*Summary of any two-step incidence, progression, and regression of diabetic retinopathy, San Luis Valley Diabetes Study, 1984–1992*

Outcome	No. at risk	No. with outcome	Cumulative 4-year incidence (%)	Incidence density per 1,000 PY (95% CI)
Incidence	169	47	22.5	63.7 (46.3–84.7)
NHW	53	17	26.2	76.1 (44.3–121.9)
Hispanic	116	30	20.8	58.3 (39.4–83.3)
Progression	75	24	24.1	68.8 (44.0–102.3)
NHW	19	7	27.2	79.3 (31.9–163.4)
Hispanic	56	17	23.0	65.2 (38.0–104.4)
Regression	75	13	13.3	35.8 (19.0–61.2)
NHW	19	6	23.5	66.9 (24.5–145.6)
Hispanic	56	7	9.7	25.6 (10.3–52.7)

Cumulative incidence is calculated directly from the incidence density rates (35). The ethnic group incidence density rates were compared via a binomial distribution test. Significance test results: for incidence, $P = 0.38$, for progression, $P = 0.66$, and for regression, $P = 0.07$.

RESULTS — Table 2 summarizes the incidence, progression, and regression rates of a two-step change in retinopathy classification by ethnicity. There were 169 people with follow-up who were negative for retinopathy at baseline. The mean age was 58.1 years, with 56.4% of this group women, 64.8% Hispanics, and a mean duration of diabetes of 4.6 years. Of the 169 subjects, 47 developed retinopathy by the second follow-up visit, giving an overall incidence rate of 63.7/1,000 person-years (PY) and a 4-year cumulative incidence of 22.5%. Hispanics had an incidence rate of 58.3/1,000 PY (4-year cumulative incidence: 20.8%), whereas the incidence rate for NHWs was 76.1/1,000 PY (4-year cumulative incidence: 26.2%). Hispanic and NHW rates were not significantly different ($P = 0.38$).

Table 3—*Comparison of subjects with no follow-up to those with follow-up by ethnicity, San Luis Valley Diabetes Study, 1984–1992*

Risk factor	NHW follow-up			Hispanic follow-up		
	No (n = 63)	Yes (n = 72)	P value	No (n = 82)	Yes (n = 172)	P value
Sex (% female)	47. 6	41.7	0.49	61.0	62.2	0.85
Age (years)	59.9	58.8	0.54	59.0	56.7	0.12
Duration of type 2 diabetes (years)	7.4	5.5	0.15	9.5	6.8	0.02
Insulin treatment (%)	31.8	21.4	0.18	50.0	36.1	0.04
Oral treatment (%)	27.0	40.0	0.11	18.8	25.4	0.24
Total GHb (%)	9.9	9.7	0.66	10.5	10.0	0.11
Systolic blood pressure (mmHg)	136.5	134.5	0.59	144.4	135.0	0.009
Diastolic blood pressure (mmHg)	78.9	78.5	0.81	80.2	79.9	0.83
BMI (kg/m^2)	27.7	29.7	0.02	28.2	29.6	0.05
Smoking ever (%)	58.7	51.4	0.39	56.1	56.4	0.96
Urine protein-to-creatinine ratio	0.15	0.10	0.02	0.24	0.13	<0.001
Family history of diabetes (%)	45.2	47.9	0.75	56.1	60.6	0.50
Total cholesterol (mg/dl)	209.9	211.3	0.87	225.9	227.7	0.78
HDL (mg/dl)	40.0	43.2	0.18	46.1	44.2	0.33
Triglycerides (mg/dl)	171.9	188.8	0.33	208.0	210.1	0.89
Retinopathy						
None (grade 10–12) (%)	55.6	73.6	<0.001	56.1	67.4	<0.001
Background (grade 15–30) (%)	22.2	23.6		17.1	22.1	
Preproliferative (grade 40) (%)	19.1	0		11.0	10.5	
Proliferative (grade 60+) (%)	3.2	2.8		15.9	0	

P values are for χ^2 tests for categorical variables and t tests for continuous variables. Triglyceride levels and the urine protein-to-creatinine ratio were log-transformed, and geometric means are presented.

Progression of retinopathy was evaluated in those who had retinopathy present at any level at baseline (n = 139), of whom 75 returned for at least one follow-up visit. The median age of this group was 58.0 years, and the group was 54.7% women, with 66.2% of Hispanic ethnicity. The mean duration of diabetes in this group was 11.9 years. Of these 75 subjects, 24 were found to have deteriorated by more than two steps in the classification. The overall progression rate was 68.8/1,000 PY, a 4-year cumulative incidence of 24.1%. Hispanics had a somewhat lower rate of progression than did the NHWs, 65.2/1,000 vs. 79.3/1,000 PY (P = 0.66), with a 4-year cumulative incidence of 23.0% and 27.2%, respectively.

Regression was less common than either incidence or progression of retinopathy, with only 13 of the 75 subjects who were positive at baseline showing improvement by at least two steps. The overall regression rate was 35.8/1,000 PY, a 4-year cumulative incidence of 13.3%. Hispanics had a regression rate of 32.9/1,000 PY (4-year cumulative incidence of 9.7%) compared with the NHWs (66.9/1,000 PY, 4-year cumulative incidence of 23.5%; P = 0.07). Of the 13 subjects who exhibited regression, 9 (69.2%) had no retinopathy detected at follow-up. None of these nine people ever exceeded a classification grade of 30.

Table 3 compares the risk factors at baseline by ethnicity for those subjects with no follow-up compared with subjects who had any follow-up. People who had no follow-up visits appeared to have more severe type 2 diabetes. They had a longer duration of diabetes and were more likely to be treated with insulin, have higher systolic blood pressure (Hispanics), and have more albuminuria. They also had more severe retinopathy at baseline.

Table 4 compares the distribution of risk factors at baseline by ethnicity for subjects free of retinopathy who had follow-up. Hispanic subjects were significantly more likely to be female and had higher total cholesterol and triglyceride levels than did NHW subjects. Hispanics were also more likely to be treated with insulin and had slightly higher GHb levels, though neither factor was statistically significant. No important differences in blood pressure, smoking, BMI, family history of diabetes, or urine protein-to-creatinine ratio were seen.

Table 5 shows the univariate association of potential risk factors for incidence of retinopathy among subjects who were negative for retinopathy at baseline and had follow-up visit(s). Higher total GHb, use of insulin, and longer total time in the study were significantly associated with increased risk of retinopathy development. People with incident retinopathy had slightly higher blood pressures and longer duration of diabetes. Hispanic ethnicity was not significantly associated with retinopathy incidence (OR = 0.74, 95% CI 0.36–1.50).

Next, the pattern of association between the risk factor variables and the development of retinopathy was assessed using both logistic regression modeling and Cox proportional hazards modeling. Nine subjects were excluded from these analyses because of missing risk factor information, leaving 160 people to analyze for any incident retinopathy. Table 6 presents the logistic regression analysis for incident retinopathy. In the full model, treatment of diabetes with insulin (OR = 9.30, 2.69–32.16, P < 0.001) and systolic blood pressure (OR = 1.81, 1.02–3.20, P = 0.04) were significantly associated with the incidence of retinopathy (Table 6, model 1). A 2% increase in GHb was associated with retinopathy incidence at near-conventional levels of significance (OR = 1.50, 0.96–2.36, P = 0.08). Treatment of diabetes with insulin was also significantly associated with incident retinopathy (OR = 8.45, 2.65–29.97, P < 0.001) after adjust-

Table 4—*Distribution of risk factors by ethnicity among subjects free of retinopathy at baseline (n = 169), San Luis Valley Diabetes Study, 1984–1992*

Participant characteristic	NHW	Hispanic	*P* value
n	53	116	
Sex (female) (%)	37.7	65.5	<0.001
Age (years)	58.7 ± 8.3	56.7 ± 10.3	0.20
Duration of type 2 diabetes (years)	3.7 ± 4.9	4.9 ± 6.4	0.18
Insulin treatment	13.7	21.1	0.26
Oral treatment	41.2	30.7	0.19
Total GHb (%)	9.0 ± 2.0	9.6 ± 2.2	0.08
Systolic blood pressure (mmHg)	134.1 ± 18.0	133.0 ± 18.2	0.72
Diastolic blood pressure (mmHg)	78.4 ± 8.2	79.7 ± 9.6	0.38
BMI (kg/m^2)	29.5 ± 5.2	29.8 ± 4.7	0.69
Smoking ever (%)	56.6	56.9	0.97
Urine protein-to-creatinine ratio	0.10 ± 0.07	0.11 ± 0.09	0.14
Family history of diabetes (%)	50.0	54.4	0.60
Total cholesterol (mg/dl)	209.0 ± 52.1	229.3 ± 45.1	0.01
Total HDL cholesterol (mg/dl)	44.0 ± 15.7	44.0 ± 15.0	0.98
Triglycerides (mg/dl)	171.8 ± 100.4	216.1 ± 124.1	0.02

Data are *n*, %, or means ± SD. *P* value is reported for the ethnic contrast using *t* test or χ^2 test. Triglyceride levels and the urine protein-to-creatinine ratio were log-transformed, and geometric means are presented with approximate standard deviations.

ment for age, sex, ethnicity, duration of diabetes, systolic blood pressure, and total GHb (Table 6, model 2). Systolic blood pressure (OR = 1.58, 0.99–2.52, *P* = 0.06) and GHb level (OR = 1.46, 0.99–2.17, *P* = 0.06) were both associated with risk of retinopathy and nearly reached conventional levels of significance. In these multiply adjusted models, Hispanic ethnicity was not significant, and a slight protective effect for developing retinopathy was suggested compared with NHW subjects (OR = 0.66, 0.28–1.57, *P* = 0.35). Duration of diabetes was negatively but not significantly associated with retinopathy incidence in model 2 (OR = 0.88, 0.60–1.29, *P* = 0.51). Removal of the diabetes treatment variable caused this association to become positive (OR = 1.18, 95% CI 0.86–1.61) with minimal changes in the other ORs, suggesting confounding of duration with insulin treatment. Time until event from baseline showed no significant effects and was removed from the models. None of the interaction terms were significant in the reduced model.

To account for variable follow-up periods, we also used Cox proportional hazards models to verify the logistic regression results. The Cox model results were similar to those from the logistic models shown in Table 6. As in the logistic model, no significant difference was seen between Hispanic and NHW subjects (hazard ratio [HR] = 0.72, 0.37–1.42, *P* = 0.34), and insulin treatment had the strongest association with incident retinopathy (HR = 4.5, 1.78–11.14, *P* value = 0.001). In the Cox model, systolic blood pressure was also significantly associated with retinopathy incidence (HR = 1.2, 1.02–1.47, *P* value = 0.03). GHb level also increased risk but did not reach conventional levels of significance (HR = 1.2, 95% CI 0.99–1.33, *P* = 0.07). Although the pattern for duration of diabetes was similar between the logistic and Cox models, it was negatively and significantly associated with retinopathy in the Cox model (HR = 0.7, 0.52–0.97, *P* = 0.03). When diabetes treatment was removed from the Cox model, the HR increased toward 1.0 (HR = 0.84, 0.64–1.11, *P* = 0.23) and was no longer significant, suggesting some degree of confounding by treatment.

The pattern of associations of risk factors and progression and regression of retinopathy was also explored; however, the models were very unstable because of the small sample sizes (data not shown).

CONCLUSIONS — We found that Hispanics had an incidence rate of 58.3/1,000 PY for new retinopathy compared with NHWs with diabetes (76.1/1,000 PY); however, the incidence

Table 5—*Univariate results for potential baseline risk factors for incident retinopathy (n = 169), San Luis Valley Diabetes Study, 1984–1992*

Risk factor (unit change)	Positive for incident retinopathy	Negative for retinopathy	OR (95% CI)
n	47	122	—
Ethnicity (Hispanic) (%)	63.8	70.5	0.74 (0.36–1.50)
Sex (female) (%)	46.8	60.7	0.57 (0.29–1.13)
Age (10 years)	56.8 ± 10.3	57.5 ± 9.5	0.93 (0.66–1.31)
Duration of type 2 diabetes (5 years)	5.5 ± 5.3	4.1 ± 6.2	1.19 (0.91–1.56)
Insulin treatment (vs. none)	39.1	10.9	5.24 (2.30–11.97)*
Oral treatment (vs. none)	34.7	33.6	1.05 (0.52–2.16)
Total GHb (2%)	10.0 ± 2.2	9.2 ± 2.1	1.45 (1.06–1.97)*
Systolic blood pressure (20 mmHg)	135.1 ± 20.7	132.7 ± 17.0	1.16 (0.80–1.67)
Diastolic blood pressure (10 mmHg)	80.2 ± 8.5	79.0 ± 9.4	1.15 (0.80–1.67)
BMI (5 kg/m^2)	28.8 ± 4.5	30.1 ± 5.0	0.74 (0.51–1.07)
Smoking ever (vs. never) (%)	63.8	54.1	1.50 (0.75–3.00)
Urine protein-to-creatinine ratio	0.12 ± 0.10	0.10 ± 0.14	1.15 (0.89–1.47)
Family history of diabetes (%)	57.4	51.3	1.28 (0.65–2.54)
Total cholesterol (50 mg/dl)	220.8 ± 42.4	223.8 ± 50.4	0.94 (0.66–1.34)
HDL (15 mg/dl)	44.9 ± 18.6	43.6 ± 13.7	1.09 (0.78–1.51)
Triglycerides (0.25 mg/dl)	191.3 ± 106.8	204.9 ± 122.3	0.88 (0.63–1.25)
Time in study (years)	5.2 (2.0–6.4)	4.5 (2.0–6.6)	1.48 (1.13–1.95)*

Data are *n*, %, or means ± SD. Unit change shows the change in the variable reflected in the OR. Triglyceride levels and the urine protein-to-creatinine ratio were log-transformed, and geometric means are presented with approximate standard deviations. Odds ratios are for 0.25 U on the log-transformed scale. Time in study is presented with the range in parentheses, instead of SD. *Statistically significant with a *P* value <0.05.

Table 6—*Analysis of risk factors for incidence of diabetic retinopathy among type 2 diabetes subjects free of retinopathy at baseline (n = 160), San Luis Valley Diabetes Study, 1984–1992*

	Model 1		Model 2	
Factor	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Ethnicity				
NHW	1.00		1.00	
Hispanic	0.63 (0.25–1.59)	0.33	0.66 (0.28–1.57)	0.35
Sex				
Male	1.00		1.00	
Female	0.57 (0.22–1.48)	0.25	0.63 (0.28–1.43)	0.27
Age (10-year increase)	0.80 (0.50–1.27)	0.34	0.86 (0.55–1.33)	0.49
Duration of type 2 diabetes (5-year increase)	0.84 (0.56–1.25)	0.38	0.88 (0.60–1.29)	0.51
Diabetes treatment				
No medications	1.00		1.00	
Insulin treatment	9.30 (2.69–32.16)	<0.001	8.45 (2.65–26.97)	<0.001
Oral treatment	2.00 (0.75–5.35)	0.17	1.88 (0.74–4.73)	0.18
Total GHb (2% increase)	1.50 (0.96–2.36)	0.08	1.46 (0.99–2.17)	0.06
Systolic blood pressure (20 mmHg increase)	1.81 (1.02–3.20)	0.04	1.58 (0.99–2.52)	0.06
Diastolic blood pressure (10 mmHg increase)	0.81 (0.47–1.38)	0.43	—	—
BMI (5 kg/m^2 increase)	0.79 (0.50–1.23)	0.29	—	—
Smoking status				
Never smoked	1.00			
Current or ever smoked	1.23 (0.53–2.84)	0.63	—	—
Urine protein-to-creatinine ratio (0.25)	1.09 (0.80–1.50)	0.58	—	—
Family history of diabetes	1.54 (0.67–3.52)	0.31	—	—
Cholesterol (50 mg/dl increase)	1.12 (0.69–1.82)	0.64	—	—
Total HDL cholesterol (15 mg/dl increase)	1.20 (0.74–1.93)	0.46	—	—
Triglycerides (0.25)	1.08 (0.67–1.77)	0.75	—	—

Table excludes nine subjects for whom treatment (2 Hispanic, 2 NHW), family history of diabetes (1 Hispanic, 2 NHW), HDL (1 Hispanic), or cholesterol and triglyceride (1 NHW) status was unknown. Triglyceride levels and the urine protein-to-creatinine ratio were log-transformed. ORs are for 0.25 U on the log-transformed scale.

rates between the two ethnic groups did not differ significantly. These incidence rates are better guides than prevalence to the true differences in retinopathy between populations, because incidence rates directly measure the risk of developing the complication over time. These results, like our prevalence data (4), suggest that Hispanics in the San Luis Valley do not have excess retinopathy risk compared with NHWs. Associations with glucose control, blood pressure, and insulin treatment were seen in both ethnic groups but did not confound the lack of difference between Hispanics and NHWs. We have also recently reported that Hispanics have no excess risk for another microvascular complication, distal symmetric sensory neuropathy (37).

Epidemiological studies that have investigated the incidence of retinopathy in several populations are summarized in Table 7. The rates ranged from 15.6/1,000 PY in Rochester, Minnesota, using routine care follow-up to 157.0/1,000 PY in the Caucasian population of the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) (38) and 170.3/1,000 PY in a small number of insulin-taking Pima Indians (17). In the present study, the overall rate of any new retinopathy development was 76.1/1,000 PY among NHWs, similar to rates seen in Denmark and Taiwan. Lower rates in our study than in the WESDR could have been due to less complete follow-up of people with more severe diabetes, use of only three-field versus seven-field photographs (39), or other factors. Because our NHW subjects were less likely to return for repeat visits, our rates are likely underestimates of the true rates in this group compared with WESDR.

The San Antonio Heart Study previously reported a higher prevalence of retinopathy in Mexican-Americans compared with NHWs (6). They found no effect of low socioeconomic status on retinopathy prevalence (16) and similar effects of glycemia, duration, insulin therapy, and blood pressure in both Mexican-Americans and Caucasians in the WESDR (40). Thus, their risk factor results are similar to ours but do not explain why they found excess prevalence in Mexican-Americans, whereas we saw no excess prevalence (4) or incidence in San Luis Valley Hispanic subjects. Differences in medical care access and therapy might be one reason, considering that Pugh et al. (41) have shown a relationship of greater retinopathy prevalence among people without health insurance or with less comprehensive ambulatory care coverage. In the San Luis Valley, medical care is generally available to people of low income through a rural community health center network. Hispanic people have nearly identical patterns of physician and hospital visits compared with NHW people in this area (data not shown). Such medical care patterns may be quite different in urban areas. Of course, other differences may exist that could alter retinopathy risk, such as unmeasured environmental, medical, or genetic factors between these Hispanic subpopulations.

In both ethnic groups, insulin therapy was positively associated with an increased incidence of retinopathy. The positive association of insulin therapy with incident retinopathy may suggest that diabetic subjects who take insulin had more severe disease. Insulin users had younger age at onset (45.9 vs. 54.0 years, $P < 0.001$), longer duration (9.2 vs. 3.5 years, $P = 0.0003$), and higher GHb levels (10.3 vs. 9.1%, $P = 0.004$), but they had a similar prevalence of hypertension (66.9 vs. 65.5%, $P = 0.77$). Systolic blood pressure and GHb level were associated with increased incidence rates of retinopathy in our study (though not reaching conventional levels of significance because of the small number of subjects), which is compatible with previous studies (13,15,17–20,42,43). The negative association of diabetes duration that was found using both the logistic (nonsignificant) and Cox (significant) models could have been an anomalous result, because those sub-

Table 7—*Comparison of studies on incidence and progression of diabetic retinopathy in subjects with type 2 diabetes*

Study (reference)	*n*	Age-group (years)	Ethnicity	Study duration (years)	Cumulative progression (%)	Cumulative incidence (%)	Incidence density (per 1,000 PY)	Methods
San Luis Valley Diabetes Study (current results)	244	20–74		4				Photographs (3 fields)*
			NHW		27.2	26.2	76.1	
			Hispanic		23.0	20.8	58.3	
			Total		24.1	22.5	63.7	
WESDR (12)	1,370	30–74	Caucasian	4	29.1	38.6	119.0	Photographs (7 fields)†
WESDR (38)	533	30–74	Caucasian	10				
		(onset at	Insulin		68.7	79.2	157.0	Photographs
		30+ years)	No insulin		52.9	66.9	110.6	(7 fields)†
Denmark (45)	215	3–90	Caucasian					Photographs
		(median 51)	Insulin	1	25.9	11.1	118.0	(2 fields) Ophthalmoscopy
Denmark (46)	273	35–92	Caucasian	1				Photographs
		(median 71)	Oral agent		21.1	7.9	82.3	(2 fields) Ophthalmoscopy
Taiwan (47)	464	40+ (mean 60.4)	Taiwanese	4	30.0	19.2	53.3	Ophthalmoscopy yearly
Rochester, MN (48)	1,031	<30 to 70+	Caucasian	4				Photographs/
			Type 2		—	6.1	15.6	Ophthalmoscopy in routine care
Pima Indian (17)	188	25+	Pima Indian	4				Ophthalmoscopy;
			Oral agent (n = 163)		—	16.7	45.7	hemorrhages plus
			Insulin (n = 25)		—	49.4	170.3	neovascularization
			Total		—	22.1	62.3	only
American Indians in Oklahoma (49)	332	All ages (mean 52)	American Indian	12.8	—	72.3	100.3	Ophthalmoscopy by specialist

*Graded with condensed Modified Airlie House classification; †graded with adaptation to Modified Airlie House classification.

jects with follow-up had type 2 diabetes for a shorter duration (6.4 vs. 8.6 years). A similar trend of reduced incidence rates with increasing diabetes duration was also noted by Klein et al. in the WESDR (38). It is possible that biological differences exist between subjects; that is, those individuals most susceptible to retinopathy will develop it rapidly, leaving those without retinopathy at a lower risk upon follow-up. Because we only explored incidence among people without retinopathy at baseline, this group may have been enriched with subjects less likely to develop retinopathy later. Further study on larger cohorts will be required to explore this observation.

A primary limitation of this study is the bias toward differential survivorship. Older subjects and those subjects with longer duration of diabetes and indications of more severe disease predominate in the group that died or did not return for follow-up. Those continuing in follow-up were younger and healthier, which may result in an underestimate of retinopathy incidence and progression. Losses to follow-up also left us with relatively small numbers at risk and reduced power to detect true associations between the risk factors and the incidence and progression of retinopathy.

In summary, although Hispanic populations have been shown to have an increased risk for type 2 diabetes itself (5,44), they do not have excess risk for microvascular complications associated with type 2 diabetes, including retinopathy and peripheral neuropathy (37) in this population. From a health services perspective, these data contribute to estimates of the risk of developing retinopathy in a population with diabetes and can serve as an estimate of need for retinopathy treatment services and for planning screening and/or treatment programs.

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