

Incidence of Diabetic Retinopathy in the Barbados Eye Studies

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Purpose: To examine the 4-year incidence and risk factors for diabetic retinopathy (DR) among black participants with diabetes in the Barbados Eye Studies (BES).

Design: Population-based incidence study.

Setting and Participants: Four hundred ten persons with diabetes mellitus (DM) from the BES cohort, which was based on a simple random sample of Barbadians, 40 to 84 years of age at baseline.

Main Outcome Measures: Development of DR, assessed by independent gradings of 30° color stereo fundus photographs of the disc and macula. Associations were evaluated by logistic regression analyses.

Results: After 4 years, DR developed in 92 of 306 (30.1%; 95% confidence interval, 25.0%, 35.5%) persons unaffected at baseline. The incidence of DR was 31.9% in those with known DM at baseline and 20.9% in newly diagnosed DM. Clinically significant macular edema developed in 16 (4.5%) of 353 individuals at risk. Seven (6.9%) of the 101 persons with minimum or moderate DR at baseline progressed to proliferative DR. Age-specific incidence declined from 36.2% at age 40 to 49 years to 28.8% and 24.2% over the subsequent two decades, increasing to 38.2% among those ≥70 years. Risk factors for DR were increased systolic blood pressure (relative risk [RR], 1.16 [1.03, 1.31]/10 mmHg increase); use of oral hypoglycemics (RR, 2.4 [1.3, 4.2]); and use of insulin (RR, 6.1 [1.7, 22.1]) (vs. no treatment or diet only); and elevated glycosylated hemoglobin (GHb; RR, 6.4 [2.5, 16.0]); GHb >11.5% vs. GHb ≤8%.

Conclusions: High rates of incident DR were evident in the black BES population, also known to have high rates of DM. Prevention of visual loss caused by DR in this population has high priority, including optimal glycemic and blood pressure control. *Ophthalmology* 2003;110:941–947 © 2003 by the American Academy of Ophthalmology.

Diabetic retinopathy (DR) is a sight-threatening ocular complication among persons with diabetes. From a public health perspective, early detection and secondary intervention are essential, because vision loss resulting from DR can usually be prevented with timely and effective treatment.^{1–3} Diabetes prevalence is higher in black than in white populations,^{4,5} but similar racial differences in DR prevalence remain inconclusive, based on the limited number of studies involving black participants.^{6–8} Incidence estimates for populations of African origin are not available to date. Most studies of DR incidence have been conducted in nonblack

populations, yielding a wide range of estimates.^{9–13} The objective of this report is to determine the 4-year incidence of DR and its associated risk factors among black participants with diabetes in the Barbados Eye Studies (BES).

Material and Methods

The BES, funded by the National Eye Institute, are a series of population-based epidemiologic studies that investigate the prevalence, incidence, and risk factors for major causes of visual loss in a large, predominantly African-origin population. The baseline prevalence study, the original BES (1988–1992), was based on a simple random sample of Barbadian-born citizens, 40 to 84 years of age, with 84% participation.¹⁴ A total of 4631 BES participants completed examinations at the study site, with 4314 (93%) self-reporting their race as black. The surviving cohort members were invited for a follow-up visit in the Barbados Incidence Study of Eye Diseases (BISED; 1992–1997) 4 years after the baseline visit (mean interval, 4 years; standard deviation [SD], 5 months). As described previously,¹⁵ 85% of the 4040 persons remaining eligible were reexamined (n = 3427: 3193 black, 139 mixed, 95 white/other). The BISED participants were younger than the non-participants (mean age, 58 years vs. 60 years), but no significant differences were found in other demographic variables, such as gender, race, and residence.

The BISED methods and protocol followed those used at baseline and have been described in detail elsewhere.¹⁵ The study

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protocol included an interview and various ocular, anthropometric, and blood pressure measurements, as well as 30° color stereo fundus photography of the disc and macula (standard fields 1 and 2 of the Diabetic Retinopathy Study).¹⁶ A systematic 10% sample and persons with positive screening findings (e.g., intraocular pressure >21 mmHg, abnormal perimetry, ocular disease, or diabetes history) were referred for a comprehensive ophthalmologic examination with dilatation. Assays of total glycosylated hemoglobin (GHb) by a column method¹⁷ were available for 3754 or 81% of the participants (GHb was not measured at the beginning of the study). Replicate testing of a random sample of laboratory determinations ($n = 264$) showed good reproducibility, with an intraclass correlation coefficient of 0.89.

Diabetes was defined by a self-reported history of physician-diagnosed diabetes mellitus (DM) and/or GHb levels >10% (i.e., at least over 2 SD above the population mean of persons without a diabetes history; mean, 7%; SD, 1.5%). Depending on age at self-reported diagnosis of diabetes, participants were further categorized as having younger (<30 years of age) or older onset (≥ 30 years). Younger-onset participants were considered to have type 1 DM if they were also receiving insulin. Older-onset participants included those with previously diagnosed type 2 DM and those newly diagnosed by the study, that is, with no diabetes history but with GHb > 10%.

Diabetic changes based on photographs of fields 1 and 2 were graded at the Fundus Photography Reading Center,¹⁸ using an adapted version of the modified Early Treatment Diabetic Retinopathy Study Airlie House classification.^{16,19} Standard fundus photographs were used to define the presence of diabetic changes, as outlined in the *ETDRS Manual of Procedures*.²⁰ These included at least three microaneurysms, retinal hemorrhages, hard and soft exudates, intraretinal microvascular abnormalities, new vessels within one disc diameter of the disc (NVD), and new vessels originating elsewhere (NVE). Other abnormalities such as clinically significant macular edema (CSME), venous beading, focal narrowing, and venous loops were noted under the category of "other." In lieu of extended retinopathy classifications, which require seven photographs, the study used a simpler classification that categorized DR into minimum, moderate, or severe in the worse eye. Minimum retinopathy was defined as the presence of ≥ 3 microaneurysms, soft or hard exudates, or retinal hemorrhages; moderate retinopathy was defined as having intraretinal microvascular abnormalities or venous beading; severe retinopathy was defined as having NVE or NVD.

All photographs were independently graded by two graders, and discrepancies were resolved by consensus. When agreement could not be reached, a retinal specialist (APS) adjudicated and determined the final grading. Evaluations of reproducibility showed good agreement for diabetic changes among the different grading teams for BES⁶ and BISED (field 1, κ , 0.76–0.81; field 2, κ , 0.78–0.81). No evidence of grading drift was found over time.

The presence of retinopathy in at least one eye was determined by the photographic gradings. The definitions of incidence and progression were as follows. Four-year cumulative incidence of DR was based on persons with diabetes and free of retinopathy at baseline, but who developed retinopathy by the 4-year follow-up. Incidence of CSME and incidence of proliferative or severe DR were similarly defined (i.e., they were based on persons with diabetes and free of CSME/proliferative DR at baseline, but who developed that specific condition by the 4-year follow-up). We also determined progression to proliferative DR, which was based on persons with diabetes and minimum or moderate DR at baseline, but who developed severe DR by the 4-year follow-up. Incidence of DR was determined according to age, gender, diabetes duration (the time period between diagnosis and the study visit), diabetes treatment, and severity.

Possible risk factors investigated included baseline age, gender, education, lifetime occupation, body mass index (weight in kg/height in m^2), waist/hip ratio, systolic blood pressure (SBP) and diastolic blood pressure (DBP; measured twice with the Hawksley random zero sphygmomanometer, and the average was used in the analysis), hypertension (SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg and/or antihypertensive treatment), smoking and alcohol use, age of onset of diabetes, as well as duration and treatment, self-reported family history of diabetes, and GHb levels. Each characteristic was first evaluated individually in a logistic regression model. Factors with a P value < 0.1 from the univariate investigation were retained in a full multivariate model. The final model included only variables with $P < 0.1$ from such evaluation. Estimates of relative risks (RR; and corresponding 95% confidence intervals [CI]) from this cohort study were based on the odds ratios derived from logistic regression models.

Results

Of the 615 black participants with diabetes and gradable fundus photographs at baseline,⁶ 147 were lost to follow-up: 45 were deceased, 4 were too ill to participate, 23 moved away/left the island, and 75 were refusals. An additional 58 persons did not have complete/gradable fundus photographs at the 4-year BISED examination, mainly because of hazy media or opacities. Among the 615 participants with diabetes, no significant differences were found between persons with and without GHb measurements with respect to baseline age, gender, reported duration of diabetes, and blood pressure. The remaining 410 participants constituted the study cohort for this follow-up evaluation. Their mean age was 57.6 years (SD, 9.4 years), and 36% were male. Table 1 compares the baseline characteristics of individuals with photographic data and those not included in this report because of death or other reasons. Persons who died during the 4-year follow-up period were older (mean age, 66.3; SD, 9.1 years), had a longer duration of diabetes, and higher SBP ($P < 0.05$) than did the participants, as indicated by t test results. Although the deceased participants were also more likely to be male and had higher GHb values than did the surviving participants, these differences were not statistically significant. Persons not included for other reasons were older (mean age, 62.7; SD, 10.4 years), tended to have higher SBP, which did not differ significantly after adjusting for age, and were similar to the participants in other characteristics.

At baseline, 104 of the 410 participants had DR, and the remaining 306 did not. Table 2 presents 4-year follow-up data on incidence and progression according to previous diagnosis. Of the 306 individuals at risk, 92 (30.1%, 95% CI based on a binomial distribution: 25.0%, 35.5%) developed incident DR. The most frequent new findings in these 306 individuals were microaneurysms (72%), retinal hemorrhages (58%), and hard and soft exudates (25%). Very infrequent findings were intraretinal microvascular abnormalities (3%), NVD/NVE (1%), or CSME (4%). When considering the distribution of diabetes type at baseline, 260 or 85% of those at risk had previously diagnosed type 2 diabetes; 43 or 14% were newly diagnosed, and only one person had younger-onset diabetes and was not on insulin (2 participants had missing data on date of onset). Among the previously diagnosed, the overall 4-year incidence was 31.9% (26.3%–38.0%) compared with 20.9% (95% CI, 10.0%, 36.0%) among the newly diagnosed; the single individual with younger-onset diabetes did not develop DR 4 years later.

As Table 2 shows, there were 353 individuals free of CSME at baseline and 16 or 4.5% (95% CI, 2.6%, 7.3%) developed incident CSME at follow-up. In addition, 407 participants did not have proliferative DR at baseline, and 2% (0.9, 3.8%) developed NVD

Table 1. Baseline Characteristics of Persons with Diabetes According to Availability of Gradable Photographs at the 4-Year Follow-Up

Baseline Characteristics	No Gradable Photographs at Follow-Up		With Gradable Photographs
	Deceased (n = 45) Mean ± Standard Deviation (Median)	Other Reasons* (n = 160) Mean ± Standard Deviation (Median)	(n = 410) Mean ± Standard Deviation (Median)
Age (yrs)	66.3 ± 9.1 (63)	62.7 ± 10.4 (63)	57.6 ± 9.4 (58)
Male, %	46.7	34.4	36.3
Duration of diabetes (yrs)	10.3 ± 10.6 (8.0)	7.4 ± 8.3 (5.0)	6.5 ± 7.2 (4.0)
SBP (mmHg)	154.9 ± 24.2 (147.0)	144.5 ± 22.1 (143.0)	139.9 ± 22.0 (138.0)
DBP (mmHg)	83.6 ± 14.0 (82.0)	82.2 ± 11.2 (81.0)	81.8 ± 12.3 (81.0)
Ghb (%)	11.8 ± 3.7 (11.6) (n = 42)	10.9 ± 3.6 (10.5) (n = 138)	10.8 ± 3.2 (10.5) (n = 360)

*For example, refusal, missing photographs, illness, and moved.

DBP = diastolic blood pressure; Ghb = glycosylated hemoglobin; SBP = systolic blood pressure.

and/or NVE after 4 years. Among the 104 participants with DR at baseline, 3 had severe retinopathy, and 101 had minimum or moderate retinopathy at baseline. Of the latter, 7 (6.9% [95% CI, 2.8%, 13.8%]) progressed to the more severe manifestations of NVD/NVE or proliferative form of DR in 4 years. All 7 progressed cases had previously been diagnosed with type 2 diabetes, with a mean duration of 11.3 years (SD, 8.7 years); 6 were treated with oral medications, whereas 1 used insulin at baseline. Further analyses are focused on the 92 persons with incident DR because of the small numbers in the other categories.

Table 3 presents age-specific and gender-specific 4-year cumulative incidence of DR. Overall incidence showed no clear trend with age, declining from 36.2% at 40 to 49 years of age to 28.8% at 50 to 59 years and 24.2% at 60 to 69 years and increasing to 38.2% at older ages. Women had a slightly higher overall incidence than did men (31.5% vs. 27.5%), although the gender difference was not statistically significant, and there was no consistent pattern by age group.

Table 4 shows incidence patterns by duration and treatment of diabetes at baseline. Incidence increased from 22.8% for persons with a duration of <4 years to 50.8% for those with a duration of 5 to 9 years. There was no increasing trend in incidence with further longer duration, although frequencies in each subcategory

were sparse. Incidence seemed higher among the small number of insulin users (7 of 12; 58.3%) than in persons treated with oral medications (34.9%) or without treatment/diet only (18.1%).

Table 5 presents risk factors for the 4-year incidence of DR in logistic regression analyses. Younger age of onset of DM was associated with higher incidence of DR (adjusted RR, 0.75). No significant associations with diabetes duration were found in multivariate logistic regression models that evaluated duration in several ways, that is, either by years of duration, a nonlinear relationship using a parabolic function, or categories of years of duration (0, 1–4, 5–9, 10–14, and ≥15 years). Persons with higher SBP had increased risk of DR (RR, 1.16 for each 10 mmHg increase in SBP). In a separate model substituting DBP for SBP, DBP also tended (RR, 1.20, $P = 0.09$) to be higher in incident cases (mean ± SD, 82.5 ± 11.2 mmHg) than in the nonincident group (80.7 ± 12.3 mmHg). Compared with persons without treatment or treated with diet only, those treated with oral medications had a RR of 2.4 for developing DR, which increased more than sixfold for persons treated with insulin (RR, 6.1). No other factors investigated were found significant, except for Ghb, as follows.

Table 6 examines the relationship between incidence of DR and Ghb among the slightly smaller subgroup of persons with Ghb data (n = 270, or 88% of the study participants). Mean (±SD) Ghb was higher among the incident than among the nonincident group (11.7% ± 3.3% vs. 9.9% ± 3.0%). The 4-year incidence increased from 10.3% in persons with Ghb ≤8% to 42.0% in those with Ghb >11.5%. After adjusting for age of onset, SBP, and treatment status, RR increased from 3.1 in persons with Ghb values between 8% and 10% to 4.7 in persons with Ghb values between 10% to 11.5%, reaching 6.4 (95% CI, 2.5, 16.0) in persons with Ghb > 11.5%. Relative risks (95% CI) for other covariates in this subgroup analysis are: 0.7 (95% CI, 0.5, 1.0) for each 10 years increase in age of diabetes onset; 1.1 (95% CI, 1.0, 1.3) for each 10 mmHg increase in SBP; 2.2 (95% CI, 1.2, 4.3) for oral medication use; and 5.4 (95% CI, 1.3, 22.3) for insulin treatment.

Table 2. Four-Year Cumulative Incidence and Progression of Diabetic Retinopathy in Black Participants with Diabetes

	No. at Risk	No. of Cases	Incidence/Progression % (95% Confidence Interval)
Incidence			
Any diabetic retinopathy	306*	92	30.1 (25.0, 35.5)
Previously diagnosed type 2	260	83	31.9 (26.3, 38.0)
Newly diagnosed type 2	43	9	20.9 (10.0, 36.0)
CSME	353	16	4.5 (2.6, 7.3)
Proliferative DR	407	8	2.0 (0.9, 3.8)
Progression to NVD/NVE	101	7	6.9 (2.8, 13.8)

*Two participants had missing data on age of onset; only one person had younger-onset diabetes.

CSME = clinically significant macular edema; DR = diabetic retinopathy; NVD = new vessels of the disc; NVE = new vessel originating elsewhere.

Discussion

Overview

The study provided a first report, to our best knowledge, on the incidence of DR among the black participants with diabetes from a large population-based investigation of ma-

Table 3. Age-specific and Gender-specific Incidence of Diabetic Retinopathy in Black Participants with Diabetes

Age (yrs) at Baseline	Men		Women		Total
	n	% (95% Confidence Interval)*	n	% (95% Confidence Interval)	% (95% Confidence Interval)
40-49	10/28	35.7 (18.6, 55.9)	15/41	36.6 (22.1, 53.1)	36.2 (25.0, 48.7)
50-59	5/29	17.2 (5.9, 35.8)	25/75	33.3 (22.9, 45.2)	28.8 (20.4, 38.6)
60-69	10/40	25.0 (12.7, 41.2)	14/59	23.7 (13.6, 36.6)	24.2 (16.2, 33.9)
70+	5/12	41.7 (15.2, 72.3)	8/22	36.4 (17.2, 59.3)	38.2 (22.2, 56.4)
Overall	30/109	27.5 (19.4, 36.9)	62/197	31.5 (25.0, 38.5)	30.1 (25.0, 35.5)

for eye diseases. Results are based essentially on persons with type 2 DM, because younger-onset diabetes was very infrequent in this population, as reported previously.⁶ In fact, only one participant in this study cohort had diabetes onset before 30 years and had been treated with oral medications. Based on a standardized photograph grading system, nearly one third (30.1%) of diabetic persons who were free of retinopathy at baseline developed new DR after 4 years (Table 2). One in 22 persons had newly developed CSME, and one in 50 persons had newly developed proliferative DR, such as NVD or NVE (Table 2). Among persons with minimum or moderate DR at baseline, 6.9% progressed to proliferative DR at the 4-year follow-up (Table 2). Incidence of DR did not seem to vary by gender or to increase with age; however, our results indicated a trend of increasing incidence with younger age of onset (Table 3). No linear trend in incidence was found with duration of diabetes (Table 4). Incidence of DR increased from 35% among persons treated with oral medications to 58% among persons treated with insulin, with adjusted RRs of 2.4 and 6.1, respectively, compared with those without medical treatment. Higher SBP and higher GHb were also found to be associated with incidence of DR (Tables 5 and 6).

Incidence of DR

Overall. Incidence estimates of DR have been discordant among various studies, a result possibly attributed to differences in study populations, methods, and definitions. In a population-based study in Minnesota, which followed a cohort of persons with diabetes from the time of clinical diagnosis onward,⁹ incidence of any retinopathy was 15.6/1000 person-years (about 6% over a 4-year period) for noninsulin dependent diabetes mellitus. The comparable

incidence was much higher in the BISED cohort, in which approximately one in five persons (20.9%) with newly diagnosed diabetes developed DR after 4 years. The Minnesota study used ophthalmoscopy for diagnosis of retinopathy, a feature that may account in part for the difference in the incidence estimates, because gradings from ophthalmoscopy and fundus photographs (used in BISED) produced only fair correlation.²¹ In addition, both study populations differed in racial composition and age, because the Minnesota study included persons younger than 40 years. A long-term (average length, 8.3 years) prospective study involving type 2 diabetic patients in Osaka, Japan,¹¹ in which DR diagnosis was determined by ophthalmologic examination, also found a much lower incidence of DR (39.8/1000 person-years). Besides the different method of diagnosis, the Japanese study population was younger (mean age, 52.1 ± 10.9 years) and had a shorter duration of diabetes (mean, 3.0 ± 4.6 years) than did those in our study.

The DR incidence in BISED seems more comparable to estimates reported from studies also using fundus photographic gradings for DR classification. In the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR), in which classification was based on 7 standard fields, the 4-year incidence of DR was 47% among the insulin users and 34% among the nonusers with age at onset ≥ 30 years.¹⁰ In a Swedish population with older-onset DM that used three fields with stereo photography of the macula in patients with no or background retinopathy and biomicroscopy in the remaining patients, the 4-year incidence was 35.6% among those who received insulin treatment and 30.8% among patients treated with oral agents and/or diet.¹² Our study findings also suggest a high incidence of DR (58%) among insulin users, but the number in the category was small (7 of 12). Combining the groups with oral medication

Table 4. Four-year Incidence of Diabetic Retinopathy by Duration and Treatment of Diabetes at Baseline

Duration (yrs) at Baseline	Treatment Status at Baseline						Overall % (95% Confidence Interval)
	None/Diet Only		Oral Medication		Insulin		
	n	% (95% Confidence Interval)	n	% (95% Confidence Interval)	n	% (95% Confidence Interval)	
<4	15/82	18.3 (10.6, 28.4)	27/112	24.1 (16.5, 33.1)	3/3	100.0 (36.8, 100.0)	22.8 (17.2, 29.4)
5-9	3/13	23.1 (5.0, 53.8)	28/46	60.9 (45.4, 74.9)	0/2	0.0 (0.0, 77.6)	50.8 (37.7, 63.9)
10-14	1/3	33.3 (0.8, 90.6)	7/18	38.9 (17.3, 64.3)	2/4	50.0 (6.8, 93.2)	40.0 (21.1, 61.3)
15+	0/6	0.0 (0.0, 39.3)	4/12	33.3 (9.9, 65.1)	2/3	66.7 (9.4, 99.2)	28.6 (11.3, 52.2)
Overall*	19/105*	18.1 (11.3, 26.8)	66/189*	34.9 (28.2, 42.2)	7/12	58.3 (27.7, 84.8)	30.1 (25.0, 35.5)

*Two had missing data on age of onset: one treated with none/diet only, one treated with oral medication.

Table 5. Associations with 4-Year Incidence of Diabetic Retinopathy

Factor	Incident Cases (n = 92)	Nonincident Group (N = 214)	Unadjusted Relative Risk (95% Confidence Interval)*	Adjusted Relative Risk (95% Confidence Interval)†
Age at baseline (yrs), mean ± SD (median)	57.1 ± 10.0 (56.0)	58.0 ± 9.2 (59.0)	0.99 (0.96, 1.02)	—
Age of diabetes onset (yrs), mean ± SD (median)	51.1 ± 10.5 (50.0)	53.6 ± 9.7 (53.5)	0.77 (0.60, 0.99)‡	0.75 (0.58, 0.99)‡
Female	67.4%	63.1%	1.2 (0.7, 2.1)	—
Diabetes duration (yrs), mean ± SD (median)	6.0 ± 6.5 (5.0)	4.3 ± 6.0 (2.0)	1.04 (1.00, 1.08)‡	—
<1	14.1%	19.3%	1.0	—
1–4	34.8%	52.4%	0.9 (0.4, 1.9)	—
5–9	33.7%	14.2%	3.3 (1.5, 7.3)‡	—
10–14	10.9%	7.1%	2.1 (0.8, 5.8)	—
15+	6.5%	7.1%	1.3 (0.4, 3.9)	—
SBP (mmHg), mean ± SD (median)	141.6 ± 22.5 (138.5)	136.4 ± 21.6 (135.0)	1.1 (1.0, 1.2)§	1.16 (1.03, 1.31)‡
Diabetes treatment				
None/diet only	20.7%	40.2%	1.0	1.0
Oral medication	71.7%	57.5%	2.4 (1.4, 4.3)‡	2.4 (1.3, 4.2)‡
Insulin	7.6%	2.3%	6.3 (1.8, 22.1)‡	6.1 (1.7, 22.1)‡

*Based on logistic regression models (univariate).

†Based on multivariate logistic regression model including age of onset, systolic blood pressure, treatment with insulin, and oral medication. Unit of change for relative risk: age of onset - 10 years; systolic blood pressure - 10 mmHg.

‡P < 0.05.

§P = 0.06.

SBP = systolic blood pressure; SD = standard deviation.

and no treatment/diet only, the 4-year incidence was 29% among all the noninsulin users in BISED. The San Luis Valley Diabetes Study (DRS fields 1, 2, and 4) found a somewhat lower 4-year cumulative incidence of 22.5% among persons with type 2 diabetes,¹³ with no significant difference between the Hispanics and non-Hispanic whites. Although BISED DR classification was based on only fields 1 and 2, more fields were used in other studies and may have attributed to the somewhat inconsistent estimates of DR incidence among these studies.

Proliferative DR and CSME. The prevalence of severe DR was uncommon (0.9%) at baseline.⁶ After 4 years of follow-up, the development of new proliferative DR remained low, only 2%, and the progression to the proliferative form of DR was 6.9%. Such an infrequent occurrence of severe DR in the Barbados population may be an underestimate as a result of higher mortality in this group, because they have an increased risk of concomitant conditions such as nephropathy or cardiovascular disease. In this re-

port, more than one fifth of the losses to follow-up were due to death, and this group had characteristics associated with worse prognosis (Table 1). Although pan-retinal photocoagulation treatment was uncommon in the population,⁶ it may affect the estimates of progression. Of the 101 persons at risk for progression to NVD/NVE, 3 had pan-retinal photocoagulation during the 4-year follow-up. All had a posttreatment status of minimum retinopathy, but if we assume these cases also represented progression to proliferative DR, the rate of progression would increase to 9.9% (95% CI, 4.9%, 17.5%). Most of these incident/progressed cases did not use insulin at baseline. Comparisons with other studies should be interpreted cautiously because of the small number of incident cases of proliferative/severe DR in BISED. The BISED incidence was generally low, however, compared with WESDR estimates of 7% and 2% among insulin users and nonusers¹⁰ and 6.8% and 5.7% in the Swedish study,¹² respectively. Consistent with our prevalence data indicating a seemingly higher frequency of CSME (8.6%) than in other populations,⁶ the 4-year incidence of CSME was 4.5% (4.2% among the noninsulin users) and seemed higher than the 2.9% incidence of macular edema found in the older-onset group not using insulin in the WESDR.²² Given the high prevalence of diabetes in this Afro-Caribbean population, the finding on CSME has potential clinical and public health relevance, because the condition is known to respond to treatment.²

Risk factors for Diabetic Retinopathy

Diabetes Duration. As duration of diabetes increased, there was no increasing linear trend toward a higher rate of newly developed DR in this study (Tables 4 and 5). Crude

Table 6. Four-Year Incidence of Diabetic Retinopathy by Baseline Glycosylated Hemoglobin Level (n = 270)

Glycosylated Hemoglobin Level at Baseline	n	Incidence %	Relative Risk (95%* Confidence Interval)
≤ 8%	7/68	10.3	1.0
>8%–10%	20/72	27.8	3.1 (1.2, 8.0)
>10%–11.5%	16/49	32.7	4.7 (1.7, 13.0)
>11.5%	34/81	42.0	6.4 (2.5, 16.0)

*Based on logistic regression model, adjusting for age of onset, systolic blood pressure, and treatment status.

incidence peaked at 5 to 9 years of duration, but the risk seemed to attenuate thereafter. The crude RR was more than threefold for persons with 5 to 9 years of diabetes, followed by nonsignificant RRs of 2.1 and 1.3 for persons with 10 to 14 years and 15 or more years of duration compared with those with diabetes diagnosed within 1 year (Table 5). However, no significant associations were found when factors such as blood pressure, diabetes treatment status, and age of onset were included in the multivariate model. Duration of diabetes has often been considered as an established risk factor for prevalence or incidence of DR, because the association has been reported by many studies.^{11,12,23-25} Nonetheless, WESDR¹⁰ found a very similar nonlinear relationship between duration and observed DR incidence to that found in our study and the Minnesota study.²⁵ Other studies also showed no significant association between duration and DR incidence.^{13,26} One possible explanation is the competing mortality for those with a lengthy illness. Reporting bias, especially among those with very long duration, could not be ruled out, because duration was calculated on the basis of self-reported age of diabetes onset. Our results, however, demonstrated an increasing trend of DR incidence toward younger age of onset, which is consistent with previous studies.^{11,25}

Blood Pressure. Elevated SBP was demonstrated as a risk factor for the incidence of DR, a compatible finding also reported in studies on nonblack populations.^{13,24,26,27} Elevated DBP was associated with the development of retinopathy only in patients treated with oral agents in the Swedish population.¹² In contrast, blood pressure was not related to the incidence of DR in persons with older-onset diabetes in WESDR²⁸ nor in populations studied in Japan¹¹ and Israel.²⁹ The association with overall hypertension, which combined both blood pressure measurements and antihypertensive treatment, was not substantiated in this study and other studies investigating such a relationship. Nonetheless, the association between SBP and development of DR found in BIASED supports the postulation that elevated blood pressure may cause some retinal exudates in diabetes.²⁴

Treatment Type. Persons treated with insulin were at sixfold increased risk of developing DR than were those without treatment or treated with diet only. The magnitude of RR was smaller, 2.4, for those treated with oral medications. Although this finding was based on very small numbers and could be due to chance, similar results were reported by other studies.^{13,26} In the San Luis Valley Diabetes Study,¹³ the corresponding RR was 8.45 (2.65-26.97) for insulin treatment and 1.88 (0.74-4.73) for oral treatment compared with no medications. Although a hazard ratio of 2.06 for initial therapy of insulin versus noninsulin was found in the Minnesota study,²⁵ their data also suggested that insulin therapy is not an independent risk factor for DR. The association may reflect the severity of the underlying disease rather than the consequence of treatment. The non-statistically significant association between duration and DR incidence, evaluated in the multivariate model, may be confounded by the strong link to the severity of diabetes as implied in the treatment status. For example, median duration of diabetes was 1 year for persons without treatment or treated

with diet only; it increased to 3 years in those treated with oral medications and 10 years in those treated with insulin.

Glycemia. Plasma glucose has been revealed as an important risk factor for DR in several epidemiologic studies.^{11,12,24-26} Instead of blood glucose, GHb was used as part of assessment for DM in the Barbados Eye Studies cohort. Results of a positive association with GHb in BIASED were consistent with such findings. Investigations by Liu and associates³⁰ concluded that GHb was slightly more associated with the prevalence and incidence of DR than was a single blood glucose determination, although no significant differences in assessing the risk for retinopathy were found. Our results also confirmed the strong relationship between level of glycemia, as measured by GHb, and incidence/progression of DR, also ascertained by others.^{13,31,32} Data from BIASED and others strongly allude to the importance of glycemic control in slowing the development/progression of DR.

Conclusions

Black populations are known to have a high prevalence of diabetes, thus providing a large number of persons at risk for the development of DR. Considering that almost one third of these persons developed DR after 4 years, it is clear that visual loss from diabetes is an important public health problem. The role of dilated examinations for early detection and treatment of DR must be carefully considered. Of the risk factors identified, both blood pressure and high GHb are potentially modifiable. Interventions to address these major factors, which increase overall morbidity and mortality, may also reduce blindness and visual impairment.

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