Nine-Year Incidence of Diabetic Retinopathy in the Barbados Eye Studies

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**Objective:** To estimate the 9-year incidence of diabetic retinopathy (DR) in a population with the same ancestry as African Americans.

**Methods:** Participants with diabetes mellitus and gradable photographs at the 9-year examination were evaluated (n=436). The incidences of minimum/moderate/severe DR, clinically significant macular edema (CSME), and sight-threatening DR (severe DR plus CSME) were defined by the development of specific diabetic changes in persons without those conditions at baseline. Progression was defined as the development of severe/proliferative DR in persons with minimum/moderate DR at baseline.

**Results:** The 9-year DR incidence was 39.6% (38.0% for minimum, 9.0% for moderate, and 2.6% for severe/proliferative DR). Incidence tended to increase with diabetes duration and treatment. Of persons with preexisting DR at baseline, 8.2% progressed to proliferative DR. The CSME incidence was 8.7%, and it increased with diabetes duration, accounting for most of the overall incidence of sight-threatening DR.

**Conclusions:** The study provides new data on long-term incidence among persons of African origin. Results suggest a possible lower risk of severe/proliferative DR than in whites, while CSME incidence seems comparable or higher. The main component of sight-threatening DR was CSME, highlighting the importance of DR as a cause of vision loss in this population.

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**DIABETIC RETINOPATHY (DR)** is a common microvascular complication in persons with diabetes mellitus (DM) and is an important cause of blindness and visual impairment in this group. Despite the high prevalence of DM, especially of type 2 DM,1-3 in persons of African origin, limited data exist on the prevalence and incidence of DR in these populations.3-6 In African Caribbean participants in the Barbados Eye Study,3 who have the same ancestral origin as African Americans, the prevalence of DR in persons with DM was nearly 30%. After 4 years of follow-up, 7% of those with DR at baseline had progressed to proliferative disease, and 30% of those unaffected at baseline had developed new DR.4 Furthermore, DR accounted for 10% of the new blindness that developed in the study cohort in this 4-year period,4 further attesting to its public health impact as a leading cause of visual loss.

As with most chronic ocular diseases, DR may develop over an extended period. Knowledge of its long-term natural history is essential to plan sound prevention and treatment strategies, yet few sources of such longitudinal data on DR exist,6,11 particularly for populations of African origin. The aim of this article is to provide information on the incidence of DR in participants with DM in the Barbados Eye Studies (BESs) after 9 years of follow-up.

**METHODS**

The BESs are a series of population-based epidemiologic studies that investigated the prevalence, incidence of, and risk factors for major causes of visual loss in a large population of predominantly African origin with funding from the National Eye Institute, Bethesda, Md. The baseline prevalence study (the BES, 1987-1992) was based on a simple random sample of Barbadian-born citizens, 40 to 84 years of age, with 84% participation. Of the 4631 persons examined at the study site, 4314 (93.2%) were black, 184 (4.0%) were mixed (black and white), and 133 (2.9%) were white or other by self-report.12 To determine the incidence and progression of these eye diseases, the surviving cohort members were invited for follow-up visits 4 and 9 years after the baseline visit in the Barbados Incidence Study of Eye Dis-
Barbados Incidence Study of Eye Diseases II (field 1: agreement for diabetic changes among different graders for the not be reached. Evaluations of reproducibility showed good indicated and determined the final grading if agreement could solved by consensus. The study retinal specialist (A.S.) adju-

proliferative DR or CSME. 

threatening DR (STDR) was defined as having severe/
sels within 1 disc diameter of the disc) in the worse eye. Sight-

proliferative (new vessels originating elsewhere or new ves-

microvascular abnormalities or venous beading), or severe/

vascular abnormalities, new vessels within 1 disc diameter of

the disc, and new vessels originating elsewhere. Abnormali-

ties noted under the category of "other" included venous bead-

ing, focal narrowing, venous loops, and clinically significant

macular edema (CSME), which was defined as (1) thickening

of the retina at or within 500 µm of the center of the macula,

(2) hard exudates at or within 500 µm of the center of the macula

associated with thickening of the adjacent retina (but not re-

sidual hard exudates remaining after the disappearance of reti-

nal thickening), and (3) a zone or zones of retinal thickening

1 disc area or larger in size, any part of which was within 1 disc

diameter of the center of the macula. Because extended reti-

nopathy classifications requiring 7 standard photographic fields

were not applicable, the study used a simpler classification that
categorized DR as minimum (≥3 microaneurysms, soft or hard
exudates, or retinal hemorrhages), moderate (intraretinal micro-
vascular abnormalities or venous beading), or severe/

proliferative (new vessels originating elsewhere or new ves-
sels within 1 disc diameter of the disc) in the worse eye. Sight-

threatening DR (STDR) was defined as having severe/

proliferative DR or CSME.

Baseline and follow-up photographs were classified inde-
dependently by 2 masked graders, and discrepancies were re-
solved by consensus. The study retinal specialist (A.S.) adju-
dicated and determined the final grading if agreement could not be reached. Evaluations of reproducibility showed good agreement for diabetic changes among different graders for the Barbados Incidence Study of Eye Diseases II (field 1: κ, 0.70-0.88; field 2: κ, 0.71-0.85), similar to those obtained for the

BES³ and the Barbados Incidence Study of Eye Diseases I.⁴ No evidence of grading drift was found across time.

Diabetic retinopathy was considered present when the photographic gradings yielded positive findings in at least 1 eye. The 9-year cumulative incidence of DR was defined as the development of DR during 9 years of follow-up based on persons with DM who were free of DR in both eyes at baseline. The incidence of CSME and the incidence by severity of DR were similarly estimated. For example, the incidence of CSME was defined as the development of CSME in either eye during the 9-year interval based on persons without CSME in both eyes at baseline. The incidence of severe DR was defined as the development of proliferative DR in 9 years based on persons without this condition at baseline. Persons at risk for incident proliferative DR included those without any DR and those with DR but with, at most, moderate DR at baseline. The incidence of STDR was considered as the development of STDR in 9 years based on persons without CSME or proliferative DR at baseline. We also determined progression to proliferative DR, which was defined as the development of severe/proliferative DR in 9 years based on persons with preexisting minimum or moderate DR at baseline. Cumulative 9-year incidence and progression rates were estimated using the product-limit approach,²⁰ which allowed the contribution of data from persons with only 4 years of follow-up. The incidence of DR was determined according to age, sex, DM duration (the period between diagnosis and the study visit), and DR severity at baseline. Relative risk ratios were based on Cox regression models with discrete time data.²¹

RESULTS

Of the 615 participants of African origin with DM and gradable fundus photographs at baseline, 436 contributed data for the 9-year incidence estimates. The remaining 179 participants had ungradable or unavailable photographs mainly because of death during the 9-year interval (n=86); other reasons included incomplete photographs, inability to photograph, refusal, or relocation overseas (n=93). Table 1 compares the baseline characteristics of the 436 participants with gradable photographic data with those with ungradable or unavailable photographs. The deceased group was the oldest (mean±SD age, 67.1±9.6 years; P=.001), as expected, and had a longer duration of DM (P=.002) and a higher systolic blood pressure than the others (P<.001). Baseline characteristics were more similar between the study cohort and those excluded for other reasons, except the latter group was older (mean±SD age, 62.1±9.8 years vs 57.6±9.4 years) and had a higher systolic blood pressure (P<.05 by 2-sample t test).

Table 2 gives the 9-year cumulative incidence and progression rates according to various baseline DR categories. A total of 324 participants had no DR at baseline and were at risk for any DR. Overall, the cumulative 9-year incidence of any DR was 39.6% (95% confidence interval [CI], 33.6%-45.5%). The incidence by DR severity was 38.0% (95% CI, 32.1%-43.9%) for minimum, 9.0% (95% CI, 5.5%-12.4%) for moderate, and only 2.6% (95% CI, 1.0%-4.3%) for proliferative DR. Among the 377 individuals free of CSME at baseline, the 9-year cumulative incidence of CSME was 8.7% (95% CI, 5.4%-12.0%). The incidence of STDR was 8.3%, very similar to that of CSME, which was its major component (given the low [2.6%] incidence of proliferative DR).
When considering DR progression to proliferative DR, 8.2% (95% CI, 2.5%-13.9%) of the 109 participants with minimum or moderate DM at baseline progressed after 9 years. Five of these 109 persons at risk had panretinal photocoagulation performed during the 9-year period. Five of these 109 persons at risk had panretinal photocoagulation performed during the baseline visit, the development of any DR in the 9-year period was 31.7%; this value increased to 58.2% when DM duration was 5 to 9 years and 60.0% when DM duration was 10 to 14 years. The trend was not maintained when DM duration was 15 years or longer (38.4%), an observation based on only 23 persons.

The incidence of CSME also increased with DM duration. Although CSME developed in approximately 1 in 20 persons having DM for less than 10 years, the incidence increased substantially when duration was longer, that is, to 20.5% for 10 to 14 years and to 26.6% for 15 years or longer. Incidence rates for STDR were similar to those for CSME and followed similar patterns because CSME is the dominating component of STDR in this population, as noted previously (Table 2).

There was an apparent gradient of any DR incidence according to DM treatment type. The lowest rate was seen in the group with none/diet treatment only, with an intermediate rate observed among users of oral medications only; the highest rate existed among insulin users (whether insulin alone or with oral medications), a group that had very few persons at risk at baseline. The incidence of CSME was also lowest in the none/diet treatment group, with higher incidence rates observed for those using oral medications only or any insulin. Compared with the none/diet treatment group, persons using oral insulin therapy were 2.4 times (95% CI, 1.4-3.9 times) more likely to develop any DR and 3.6 times (95% CI, 1.1-12.2 times) more likely to develop CSME.

The previous diagnosis of type 2 DM was not strongly related to the incidence of any DR. The latter rate was only slightly higher among those with previously diagnosed type 2 DM at baseline (40.4% vs 33.9%). In contrast, the incidence of CSME tended to double when type 2 DM had been previously diagnosed (9.3% vs 4.1%), although this finding was not statistically significant (relative risk ratio, 1.8; 95% CI, 0.4-7.9). Younger-onset DM is infrequent in the population. Among persons at risk for any DR, only 1 had younger-onset DM at baseline; this individual developed DR during the 9-year follow-up. Three persons with younger-onset DM were at risk for CSME or STDR, and 1 developed DR in 9 years.

This study provides new information on the long-term occurrence of DR in a large population of predominantly African origin in which nearly 20% of the population has DM (mainly type 2 DM). Based on a standardized photograph grading system and a 9-year follow-up, DR developed in approximately two fifths of the participants with DM who were free of DR at baseline.
The 9-year cumulative incidences of CSME and proliferative DR were 8.7% and 2.6%, respectively, with an overall incidence of 8.3% for STDR, that is, development of either or both conditions. Among persons with preexisting minimum or moderate DR at baseline, 8.2% progressed to proliferative DR. The rate would increase to 12.9% if persons treated with panretinal photocoagulation between baseline and the 9-year follow-up visit were included (ie, assuming they had progressed to proliferative DR before treatment).

The cumulative 9-year incidence of DR was highest in the youngest and oldest age groups; DR developed in nearly half (47.0%) of persons aged 40 to 49 years and in more than three fifths (62.3%) of those 70 years or older. A slightly higher incidence was observed in women (41.8%) than in men (35.3%), but the difference was not statistically significant. The risk of DR was most manifest in persons with a DM duration of 5 years or longer, whereas a DM duration of 10 years or longer coincided with a substantial increase in CMSE and STDR risk.

Table 3. The Age- and Sex-Specific 9-Year Incidence of Diabetic Retinopathy in Participants With Diabetes Mellitus

<table>
<thead>
<tr>
<th>Age at Baseline, y</th>
<th>No. at Risk</th>
<th>Incidence, % (95% CI)</th>
<th>No. at Risk</th>
<th>Incidence, % (95% CI)</th>
<th>No. at Risk</th>
<th>Incidence, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-49</td>
<td>30</td>
<td>33.3 (16.5-50.2)</td>
<td>43</td>
<td>53.1 (37.7-68.5)</td>
<td>73</td>
<td>47.0 (34.8-59.3)</td>
</tr>
<tr>
<td>50-59</td>
<td>31</td>
<td>32.1 (14.6-49.7)</td>
<td>78</td>
<td>41.0 (29.4-52.6)</td>
<td>109</td>
<td>38.6 (28.9-48.3)</td>
</tr>
<tr>
<td>60-69</td>
<td>43</td>
<td>36.1 (16.7-55.4)</td>
<td>64</td>
<td>27.3 (15.4-39.1)</td>
<td>107</td>
<td>30.0 (20.0-40.0)</td>
</tr>
<tr>
<td>≥70</td>
<td>13</td>
<td>38.5 (12.0-64.9)</td>
<td>22</td>
<td>78.8 (44.2-100.0)</td>
<td>35</td>
<td>62.3 (33.6-90.9)</td>
</tr>
<tr>
<td>Overall</td>
<td>117</td>
<td>35.3 (25.4-45.3)</td>
<td>207</td>
<td>41.8 (34.4-49.2)</td>
<td>324</td>
<td>39.6 (33.6-45.5)</td>
</tr>
</tbody>
</table>

Abbreviation: CI, confidence interval.

Table 4. The 9-Year Incidence of Any DR, CSME, and STDR by Duration, Treatment, and Type of Diabetes Mellitus at Baseline

<table>
<thead>
<tr>
<th>Status of Diabetes at Baseline</th>
<th>Any DR</th>
<th>CSME</th>
<th>STDR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. at Risk</td>
<td>Incidence, %</td>
<td>No. at Risk</td>
</tr>
<tr>
<td>Duration, y*</td>
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<td></td>
<td></td>
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<tr>
<td>≤4</td>
<td>209</td>
<td>31.7</td>
<td>221</td>
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<tr>
<td>5-9</td>
<td>65</td>
<td>56.2</td>
<td>78</td>
</tr>
<tr>
<td>10-14</td>
<td>25</td>
<td>60.0</td>
<td>36</td>
</tr>
<tr>
<td>≥15</td>
<td>23</td>
<td>38.4</td>
<td>39</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None/diet only</td>
<td>111</td>
<td>26.0</td>
<td>114</td>
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<tr>
<td>Oral medication only</td>
<td>201</td>
<td>44.8</td>
<td>242</td>
</tr>
<tr>
<td>Any insulin</td>
<td>12</td>
<td>100.0</td>
<td>21</td>
</tr>
<tr>
<td>Type*</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Newly diagnosed type 2</td>
<td>47</td>
<td>33.9</td>
<td>49</td>
</tr>
<tr>
<td>Previously diagnosed type 2</td>
<td>274</td>
<td>40.4</td>
<td>322</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; CSME, clinically significant macula edema; DR, diabetic retinopathy; STDR, sight-threatening DR.

*Among persons at risk for any DR, 2 had missing data on age at onset; only 1 person had younger-onset diabetes. Among persons at risk for CSME or STDR, 3 had missing data on age at onset and 3 had younger-onset diabetes.

LONG-TERM ESTIMATES OF DR INCIDENCE ARE AVAILABLE FROM ONLY A FEW STUDIES, AND NONE ARE FROM AFRICAN-DERIVED POPULATIONS. RATES FROM THOSE STUDIES CANNOT BE COMPARED DIRECTLY WITH OUR RATES BECAUSE DIFFERENCES EXIST IN POPULATIONS (EG, DEMOGRAPHIC COMPOSITION OR RELEVANT CLINICAL CHARACTERISTICS AT BASELINE) AND METHODS (EG, OVERALL DESIGN, DEFINITIONS, OR DATA COLLECTION METHODS). ONE OF THOSE STUDIES IS THE WISCONSIN EPIDEMIOLOGIC STUDY OF DIABETIC RETINOPATHY (WESDR), WHICH REPORTED A 10-YEAR DR INCIDENCE OF 79% FOR INSULIN USERS AND 67% FOR NONINSULIN USERS IN PERSONS WHOSE CONDITIONS WERE DIAGNOSED AT 30 YEARS OR OLDER.8 IN OUR STUDY COHORT, A HIGH 9-YEAR INCIDENCE (100%) WAS ALSO FOUND AMONG THE FEW INSULIN USERS AT RISK (N=12). HOWEVER, MOST OF OUR PARTICIPANTS, WHO DID NOT USE INSULIN, HAD A MUCH LOWER INCIDENCE (38.2%; 95% CI, 32.1%-44.2%) THAN IN THE WESDR. BECAUSE THE WESDR INCLUDED PROMINENTLY EUROPEAN-DERIVED PARTICIPANTS FROM A NORTHERN US LOCATION, UNDERLYING DIFFERENCES IN POPULATION COMPOSITION, LIFESTYLE, ENVIRONMENTAL FACTORS, AND HEALTH CARE PATTERNS EXIST BETWEEN THE STUDIES. THE DISCREPANT ESTIMATES MIGHT ALSO BE PARTLY EXPLAINED BY POSSIBLE VARIATIONS IN THE SEVERITY OF THE CASE MIX AT BASELINE AND BY THE EXTENT OF GYMIC CONTROL OF THE PARTICIPANTS. UNLIKE THE WESDR, WHICH WAS BASED ON PATIENTS WITH DM WHO WERE RECEIVING MEDICAL CARE AT BASELINE, OUR STUDY WAS BASED ON PERSONS WITH DM IDENTIFIED FROM A REPRESENTATIVE RANDOM SAMPLE OF THE POPULATION OF THE COUNTRY. AS A RESULT, IT POSSIBLY INCLUDED MORE PERSONS WITH NEWLY DIAGNOSED AND EARLIER STAGES OF DM THAN THE WESDR, THEREBY LEADING TO A LOWER INCIDENCE OF DR. THIS
may be a partial explanation, as approximately two thirds of our cohort had a DM duration of less than 5 years vs approximately 14 years in the WESDR. In terms of DM duration, our population seems more comparable with the older-onset noninsulin users in the WESDR, who had an average DM duration of 7 years.8 Still, even in the subgroup using oral DM treatment only, the 9-year incidence from our study (44.8%) was considerably lower than the WESDR rate. Another important difference between studies was that we used a simple DR classification based on 2 standard fields, whereas the WESDR used a DR classification based on 7 standard fields, which could be more sensitive to detecting lesions. However, a study22 from the WESDR showed that the sensitivity of 2 fields for detecting any DR compared with 7 fields was high at 87%. When estimating incidence rates using 2 vs 7 fields, possible underestimation could occur for the numerator (number of incident cases), whereas overestimation could occur for the denominator (number at risk). Although it is not possible to compute accurate estimates that account for these potential issues, simple linear extrapolation suggested that if 7 fields had been used in the BESs, the 10-year incidence among the noninsulin users in our population would be approximately 36%, an estimate that remained lower than that in the WESDR.

In contrast to the WESDR, a much lower incidence of DR than in our study was reported in the Hoorn Study,11 a population-based cohort study in the Netherlands that included persons aged 50 to 74 years. After an average follow-up of 9.4 years, the cumulative incidence of DR, determined using ophthalmoscopy and fundus photography, was 13.6% in individuals with impaired glucose metabolism and 17.5% in those with DM. The numbers at risk in this study were small, however, being 66 and 57 for the respective groups.11 Losses to follow-up were also considerable and may have resulted in the selective participation of a healthier, low-risk group. Comparisons must also consider the differences in classifications used in that study and ours.

The presence of retinopathy in persons without DM has been reported in various populations.3,11,22-28 Although the main focus of the present study pertained to the incidence of DR in persons with DM, we also examined the incidence in those without DM. A relatively low 9-year cumulative incidence of any retinopathy was found in black participants who did not meet the criteria for DM (3.3%; 95% CI, 2.2%-4.4%).

PROLIFERATIVE DR

In the BESs, we found that the development of new proliferative DR after 9 years was 2.6% (3.8% when including those with photocoagulation treatment); most persons with incident proliferative DR had some DR at baseline. In contrast, 10% of older-onset noninsulin users in the WESDR (free of such lesions at baseline) had proliferative DR after 10 years. The low incidence of 2.6% in our study might reflect selective mortality in the cohort due to the increased risk of comorbidities such as nephropathy and cardiovascular disease, as delineated previously.3,4 In addition to older age, persons excluded because of ungradable/ unavailable photographs had a longer DM duration and higher blood pressure, possibly also leading to selective mortality and further contributing to underestimation of the true incidence. Underascertainment could have occurred if persons at higher risk for proliferative DR tended to have fewer gradable photographs, eg, because of cataract. Another possible explanation is that gradings were based on 2 fields, which had a 74% sensitivity to detect proliferative DR in the WESDR (vs 7 fields).27 However, after accounting for the 74% WESDR sensitivity of 2 fields, the resulting BESs estimate is only 5.3%, if followed for 10 years. These results continue to suggest a much lower incidence of proliferative DR in the BESs than in the WESDR, which is based on participants of predominantly European origin. Furthermore, the low long-term incidence of proliferative DR in the BESs is consistent with previous findings of a low prevalence of severe DR at baseline (0.9%)3 and the low risk of new proliferative DR at the 4-year follow-up visit (2%).3 These findings could suggest that the development of the more severe type of DR in this population of African origin is relatively infrequent.

CSME AND STD

Our prevalence and earlier follow-up results4 suggest a higher prevalence and 4-year incidence of CSME in this cohort than in other groups. The present findings continue to support the high occurrence of CSME in this population, in which approximately 1 in 11 persons with DM developed CSME in a 9-year period. In the WESDR,28 the 10-year incidence of CSME was estimated to be 11.1% in patients with DM treated with oral medications; the comparable 9-year incidence in our study was 11.3%, a follow-up interval that is 1 year shorter. As opposed to the relatively lower incidence rates of any DR and of proliferative DR in our study than in the WESDR, the incidence of CSME seemed to be at least at the WESDR levels, despite the limitations inherent in comparing the 2 studies.

The patterns of STD incidence paralleled those of CMSE, which was its major component. As discussed previously, proliferative DR was relatively infrequent in our study population.

STRENGTHS AND LIMITATIONS

This study provides new information on the development of DR in persons of African origin during a 9-year period. Factors related to the long-term incidence of DR are discussed in a separate article.29 The major strengths of this study are its population-based design and long-term follow-up, which allow ascertainment of natural history. An additional strength is that the presence of DR was determined by independent grading of fundus photographs based on a standardized system. Gradings were based on disc and macula photographs, reported to capture 87% of any diabetic changes present in 7 photographic fields. As in all cohort studies, a potential weakness relates to the inevitable losses to follow-up from various causes, such as mortality. This issue is particularly relevant in cohort studies based on persons with DM, who are at higher risk for death. If selective mortality applies to subgroups of individuals with DM, for example,
persons with more severe DM or a longer DM duration, underestimation of DR incidence may occur. A similar issue arises from incompleteness of data on fundus photographs. Because DM and age-related cataract often coexist, individuals with missing photographs are likely to be older and to have a longer duration of DM. Furthermore, elevated blood pressure may increase the likelihood of DR development. Therefore, the inability to include their data in the analyses may also lead to underestimation of the rates, particularly in the older age groups, those with extended DM duration, and those with hypertension. Interpretation of our findings should consider these potential issues.

CONCLUSIONS

This longitudinal study provides new data on the frequency and patterns of DR development during an extended period that has been unavailable to date for persons of African descent. After 9 years, two fifths of the participants with DM developed new DR, and although the risk of proliferative DR seemed lower than in other studies, CSME risk may be comparable or higher. This information has clinical and public health implications, particularly given the high frequency of DM in populations of African origin and the potential to prevent some DR-related vision loss with early treatment. These results highlight the need to develop programs to avoid the sight-threatening complications of DM, particularly in high-risk populations.