Glycemic and Blood Pressure Control in an Asian Malay Population With Diabetes and Diabetic Retinopathy

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Objective: To examine the prevalence of and factors associated with suboptimal glycemic and blood pressure (BP) control in a Malay population with diabetes mellitus in Singapore.

Methods: The Singapore Malay Eye Study was a population-based survey of 3280 Malay individuals (78.7% response rate) aged 40 to 80 years. Diabetes was defined as a nonfasting glucose level of 200 mg/dL or greater, use of diabetic medication, or physician diagnosis. Diabetic retinopathy (DR) was graded from retinal photographs using the modified Airlie House classification. Optimal control was defined as a hemoglobin A1c level of less than 7% and BP of 130/80 mm Hg or lower.

Results: In participants with diabetes (n=768), only 26.9% had optimal glycemic and 13.4% optimal BP control, respectively. In those with DR (n=272), rates of optimal glycemic and BP control were even lower (17.4% and 10.3%, respectively). After adjusting for age, sex, socioeconomic status, and other factors, compared with participants with optimal glycemic control, those with suboptimal control were younger (P=.005), more likely to be unaware of their diabetes status (P<.001), and taking medication for diabetes (P<.001) and had higher levels of total cholesterol (P=.009) and DR (P<.001). After adjusting for similar risk factors, compared with participants with optimal BP control, those with suboptimal BP control were older (P=.006) and more likely to have higher total cholesterol levels (P=.002), BMIs (P=.04), and DR (P=.02).

Conclusions: In this Asian Malay population with diabetes, more than three-quarters had poor glycemic and BP control. Strategies to improve awareness and implement evidence-based guidelines are needed to reduce the effect and burden of diabetic complications in Asia.

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40-49, 50-59, 60-69, and 70-79 years) totaling an initial 5600 names were selected. Of these, 4168 individuals (74%) were eligible to participate. A person was considered ineligible if he or she had moved from the residential address, had not lived there in the past 6 months, was deceased, or was terminally ill. Of 4168 eligible individuals, 3280 participants took part in our study (78.7% participation rate). Of the nonparticipants, 831 (20%) declined to participate and 57 (1%) could not be contacted. Nonparticipants tended to be in the older age group (70-79 years) compared with participants but there were few other differences in sex, sampling location, and telephone ownership.

Of the 3280 participants, we included 768 who had diabetes, defined by a random glucose level of 200 mg/dL or higher (to convert to millimoles per liter, multiply by 0.0555), use of diabetic medication, or a previous physician diagnosis of diabetes.10 The study was approved by the hospital institutional review board and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants.

**ASSESSMENT OF HEMOGLOBIN A1C AND BP**

Nonfasting venous blood samples (3 mL) were drawn and sent for analysis of glycated hemoglobin levels (HbA1c) at the National University Hospital Reference Laboratory11 using a high-performance liquid chromatography cation exchange system implemented on a Bio-Rad variant II analyzer (Hercules, California).

The HbA1c assay was accredited by the National Glycoprotein Standardization program with controls traceable to the Diabetes Control and Complications Trial.11

A digital automated BP monitor (Dinamap model Pro DP110X-RW, 100V2; GE Medical Systems Information Technologies, Milwaukee, Wisconsin) was used to measure seated BP on 2 occasions, 5 minutes apart. If the BP differed by more than 10 mm Hg systolic and 5 mm Hg diastolic, a third measurement was taken. The BP was recorded as the mean of the 2 closest readings.

Optimal control of HbA1c and BP was described based on World Health Organization and the American Diabetes Association guidelines12 (optimal HbA1c, <7%; suboptimal HbA1c, ≥7% [to convert to proportion of total hemoglobin, multiply by 0.01] and optimal BP, ≤130/80 mm Hg; suboptimal BP, >130/80 mm Hg). The HbA1c levels were divided into 4 subcategories for further analyses: 6.5% or lower, 6.5% to 7.0%, 7.0% to 8.0%, and greater than 8.0%.

**ASSESSMENT OF DIABETIC RETINOPATHY**

Diabetic retinopathy (DR) was assessed using standardized dilated retinal photography,1 performed using a digital retinal camera (Canon CR-Di; 10D SLR back, Tokyo, Japan). Two retinal photographs, centered at the optic disc and macula, were taken from both eyes of each participant. Diabetic retinopathy was considered present if any characteristic lesions, as defined by the Early Treatment Diabetic Retinopathy Study, were found: microaneurysms (MA), hemorrhages, cotton wool spots, intraretinal microvascular abnormalities, or venous beading; level 41, microaneurysms and 1 or more of cotton wool spots or intraretinal microvascular abnormalities less than standard photograph 8A; level 51, microaneurysms and 1 or more of venous beading, hemorrhage, microaneurysms of standard photograph 2A or more, or intraretinal microvascular abnormalities of standard photograph 8A or more; level 61, fibrous proliferation; level 61 through 64, laser scatter photocoagulation scars with retinopathy levels 31 through 51; level 65, proliferative diabetic retinopathy less than high-risk characteristics, as defined in the Diabetic Retinopathy Study; level 70, proliferative diabetic retinopathy with high-risk characteristics; and level 80, total vitreous hemorrhage. Macular edema was defined by hard exudates in the presence of MA and blot hemorrhage within 1 disk diameter of the foveal center or focal photocoagulation scars in the macular area.

We defined 4 primary outcomes as minimal DR, level 15 to 20; mild DR, level 35; moderate DR, level 43; and severe nonproliferative DR, level 47-90 (macular edema).

**ASSESSMENT OF OTHER PATIENT FACTORS**

A standardized questionnaire was administered to obtain demographic data, lifestyle risk factors, and medical history. Low socioeconomic status comprised 2 criteria: (1) primary education or less and (2) an individual monthly income less than SGD $2000. History of stroke and acute myocardial infarction was based on self-report. Chronic kidney disease was defined as an epidermal growth factor receptor level of less than 80 mL/min/1.73 m², consistent with the US National Kidney Foundation Kidney Disease Outcome Quality Initiative working group definition.11 Peripheral artery disease was defined as an ankle brachial index of 0.9 or less in at least 1 leg. Ankle brachial index was defined as the ratio of the higher of 2 systolic pressures (from posterior tibial and dorsalis pedis) at the ankle to the average of the right and left brachial artery pressures. A 40-mL sample of venous blood was collected and sent to the National University Hospital Laboratory to determine serum cholesterol levels.9

Other ocular factors were also documented. Cataract was graded using the Wisconsin Cataract Grading System from digital photographs taken after pharmacologic (tropicamide, 1%, and phenylephrine hydrochloride, 2.5%) dilation. Posterior subcapsular cataract was defined by presence of typical opacity present at the posterior part of the lens.13

**STATISTICAL ANALYSIS**

Analyses were performed in SPSS version 15 (SPSS Inc, Chicago, Illinois). Baseline characteristics of participants with and without DR were compared using descriptive statistics. The Pearson χ² test was used to compare proportions of categorical variables (eg, sex), while independent samples t tests were used to compare means and standard deviations of continuous variables (eg, HbA1c) after checking variances using the Levene Test for Equality of Variances. Multivariable-adjusted odds ratios (OR) and 95% confidence intervals (CI) were calculated for factors associated with suboptimal glycemic or BP control using logistic regression models. At prespecified α = .05, the power to detect a minimum positive trend in the percentage of patients with suboptimal BP control is 98.2%. Likewise, the power to detect a positive trend in the proportion of patients with suboptimal HbA1c control is 88.6%.
RESULTS

Of 768 participants with diabetes, 99.1% (n = 761) had gradable retinal photographs, 97.3% (n = 747) had measured HbA1c levels, and 99.7% (n = 766) had measured BP levels. The prevalence of DR was 35.4%. Figure 1 shows the breakdown of DR grades, showing that nearly 1 in 10 had severe DR.

Table 1 shows characteristics of the study sample. The mean (SD) age was 62.5 (9.4) years, and the mean (SD) diabetes duration was 12.1 (8.7) years, with 58.3% of patients (n = 448) taking oral hypoglycemic agents, 10.3% (n = 81) taking insulin, and 41.5% (n = 318) taking antihypertensives. Compared with participants without DR, those with DR were more likely to have longer duration of diabetes (P < .001), being insulin treatment (P < .001), and have suboptimal control levels of HbA1c (P < .001) and BP (P < .001).

Overall, the mean HbA1c level was 8.0% (range, 4.5%-15.1%), with only 26.9% (95% CI, 23.8%-30.0%) having an optimal HbA1c level. In participants with DR, only 17.4% had an optimal HbA1c level. Figure 2 shows proportions by each category of glycemic control in participants with and without DR. An HbA1c level greater than 8% was present in 49.1% of the overall sample (42.6% and 61.9% of persons with and without DR, respectively). Persons with HbA1c levels greater than 8% were more likely to have DR (P < .001) compared with persons with an HbA1c level lower than 8%.

Mean systolic BP and diastolic BP levels were 154.6 and 79.2 mm Hg, respectively, with optimal BP levels achieved in 13.4% of patients (n = 1102). Mean (SD) diabetes duration was 12.1 (8.7) years, with 58.3% (95% CI, 50.0%-76.6%) taking oral hypoglycemic agents, 10.5% (n = 81) taking insulin, and 41.5% (n = 318) taking antihypertensives. Compared with participants without DR, those with DR were more likely to have longer duration of diabetes (P < .001), being insulin treatment (P < .001), and have suboptimal control levels of HbA1c (P < .001) and BP (P < .001).

The associations of patient characteristics with suboptimal glycemic (HbA1c ≥ 7%) and BP (BP > 130/80 mm Hg) control are shown in Table 2 after adjusting for age, sex, socioeconomic status, and other factors. Factors associated with higher odds of suboptimal glycemic control included higher serum cholesterol levels (OR, 1.33; 95% CI, 1.05-1.68; P = .02), being previously undiagnosed with diabetes (OR, 7.65; 95% CI, 3.23-18.11; P < .001), being treated with oral hypoglycemic agents (OR, 3.47; 95% CI, 1.82-6.60; P < .001), and having DR (OR, 2.42; 95% CI, 1.63-3.59; P < .001). Older age was associated with decreased odds of suboptimal glycemic control (OR, 0.97; 95% CI, 0.93-0.99; P = .003).

Factors associated with higher odds of suboptimal BP included older age (OR, 1.04; 95% CI, 1.00-1.07; P = .03), male sex (OR, 1.98; 95% CI, 1.14-3.44; P = .01), higher

### Table 1. Characteristics of Participants With Diabetes in the Singapore Malay Eye Study

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Persons With Diabetes (n=768)</th>
<th>Diabetic Retinopathy (n=272)</th>
<th>P Value a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>62.5 (9.4)</td>
<td>62.8 (9.8)</td>
<td>61.9 (8.6)</td>
</tr>
<tr>
<td>Duration of diabetes, y</td>
<td>12.1 (8.7)</td>
<td>10.4 (7.8)</td>
<td>15.0 (9.4)</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>154.6 (23.7)</td>
<td>152.1 (22.8)</td>
<td>159.4 (24.5)</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td>79.2 (11.0)</td>
<td>79.2 (10.5)</td>
<td>79.2 (11.8)</td>
</tr>
<tr>
<td>Optimal HbA1c, %</td>
<td>103.1 (13.4)</td>
<td>73 (15.0)</td>
<td>28 (10.3)</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>212.4 (50.2)</td>
<td>212.4 (46.3)</td>
<td>208.5 (54.0)</td>
</tr>
<tr>
<td>HDL cholesterol, mg/dL</td>
<td>50.2 (11.6)</td>
<td>50.2 (11.6)</td>
<td>50.2 (11.6)</td>
</tr>
<tr>
<td>Triglycerides, mg/dL</td>
<td>168.1 (141.6)</td>
<td>159.3 (132.7)</td>
<td>177.0 (168.1)</td>
</tr>
<tr>
<td>Serum glucose, mg/dL</td>
<td>198.2 (90.1)</td>
<td>191.0 (86.5)</td>
<td>216.2 (108.1)</td>
</tr>
<tr>
<td>BMI</td>
<td>27.4 (4.8)</td>
<td>27.7 (5.0)</td>
<td>27.0 (4.4)</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); BP, blood pressure; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SGD, Singapore dollar.

SI Conversion: To convert percentage to proportion of total hemoglobin, multiply by 0.01; cholesterol to millimoles per liter, multiply by 0.0259; triglycerides to millimoles per liter, 0.0113; glucose to millimoles per liter, 0.0555.

a Numerals in boldface indicate statistical significance at P < .05.

b Optimal HbA1c indicates an HbA1c level less than 7%; optimal BP, 130/80 mm Hg or less.
COMMENT

Good glycemic and BP control are modifiable factors that reduce vascular complications of diabetes. Our study provides population-based data showing that only 1 in 4 Malay persons with diabetes in Singapore achieved optimal glycemic control and 1 in 8 achieved optimal BP control. Among persons with DR, these proportions were even lower (1 in 6 and 1 in 10, respectively). We further demonstrated that factors associated with suboptimal glycemic control included younger age, higher total cholesterol levels, a lack of knowledge of diabetes diagnosis, taking oral hypoglycemic agents, and the presence of DR, while factors associated with suboptimal BP control included older age, higher total cholesterol levels, higher body mass index, presence of DR, and presence of posterior subcapsular cataract, and not having a previous acute myocardial infarction.

The low proportion (26.9%) of patients who achieved optimal glycemic control in our study is consistent with population17 and clinic-based studies17,18 conducted in Western countries suggesting that less than 40% of persons with diabetes achieved recommended glycemic and BP targets. In particular, the National Health and Nutrition Examination Survey,2 which surveyed noninstitutionalized US citizens, found that only 37% and 36%, respectively, achieved targets levels of HbA1c of less than 7% and BP of 130/80 mm Hg or lower. Further analysis of the same sample in Australia demonstrated poor patient knowledge of HbA1c,21 and the

Our study also provides data on an Asian subpopulation nearly 10 years after the Diabcare-Asia 1998,7 a large study of 12 Asian nations including Singapore that documented poor achievement of glycemic targets. We noted that the mean HbA1c levels and proportions of patients with HbA1c greater than 8% documented in the previous study were similar to the results of our current study. The mean (SD) HbA1c levels of 8.0% (1.9%) and 55% of patients with HbA1c levels greater than 8% in their study were comparable with the mean (SD) HbA1c levels of 8.0% (2.0%) and 49.1% of patients with HbA1c levels greater than 8% in our sample. This comparison indicates that, in Asian countries, glycemic control remains a major challenge in diabetes management.

A recent meta-analysis based largely on studies in Western populations suggested that improving glycemic control in the management of diabetes in the last decade may have contributed to a decline in the progression of severe DR and incidence of vision loss.19 In the United Kingdom Prospective Diabetes Study, a reduction of HbA1c level from 7.9% to 7.0% resulted in risk reduction of the need for retinal photocoagulation by 29%, the progression of vitreous hemorrhage by 17%, and blindness by 16%.3 The recent ADVANCE Retinal Measurements study reported 12.2%, with progression of 2 or more steps in the Early Treatment Diabetic Retinopathy Study classification of DR, compared with 27.8% (for 6 years) reported by the United Kingdom Prospective Diabetes Study. This difference can likely be attributed to improved diabetes care since the United Kingdom Prospective Diabetes Study, as reflected by higher levels of medication use in the ADVANCE Retinal Measurements study population compared with the United Kingdom Prospective Diabetes Study population.22

A few studies have investigated glycemic and BP control in clinic patients with DR. A survey of 483 patients with DR conducted in Australia24 documented slightly lower proportions with optimal glycemic control (14% vs 17.4% in our sample) but higher proportions with optimal BP control (18% vs 10.3%) compared with findings from our sample. Further analysis of the same sample in Australia demonstrated poor patient knowledge of HbA1c,21 and the
Table 2. Characteristics Associated With Suboptimal Levels of Glycemic and Blood Pressure Controla

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Suboptimal HbA1c</th>
<th>P</th>
<th>Multivariable ORd</th>
<th>P</th>
<th>Suboptimal BP</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>Age-Sex ORb</td>
<td>95% CI</td>
<td>P Valuec</td>
<td>Age-Sex ORb</td>
<td>95% CI</td>
<td>P Valuec</td>
</tr>
<tr>
<td></td>
<td>(95% CI)</td>
<td></td>
<td></td>
<td>(95% CI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>0.96 (0.94-0.98)</td>
<td>.001</td>
<td>0.97 (0.95-0.99)</td>
<td>.003</td>
<td>1.04 (1.01-1.06)</td>
<td>.002</td>
</tr>
<tr>
<td>Male vs female sex</td>
<td>1.19 (0.85-1.66)</td>
<td>.32</td>
<td>1.12 (0.76-1.64)</td>
<td>.56</td>
<td>0.98 (0.64-1.50)</td>
<td>.92</td>
</tr>
<tr>
<td>Low SES</td>
<td>0.72 (0.50-1.04)</td>
<td>.08</td>
<td>0.70 (0.47-1.04)</td>
<td>.08</td>
<td>1.64 (0.96-2.81)</td>
<td>.07</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>1.27 (1.11-1.47)</td>
<td>.001</td>
<td>1.33 (1.05-1.68)</td>
<td>.02</td>
<td>1.63 (1.21-2.18)</td>
<td>.001</td>
</tr>
<tr>
<td>Newly diagnosed diabetes</td>
<td>2.49 (1.35-4.60)</td>
<td>.004</td>
<td>7.65 (3.23-18.11)</td>
<td>&lt;.001</td>
<td>1.72 (0.85-3.45)</td>
<td>.13</td>
</tr>
<tr>
<td>Family history</td>
<td>0.82 (0.58-1.15)</td>
<td>.25</td>
<td>.....</td>
<td>.....</td>
<td>0.59 (0.38-0.91)</td>
<td>.02</td>
</tr>
<tr>
<td>BMI</td>
<td>1.00 (0.96-1.04)</td>
<td>.93</td>
<td>.....</td>
<td>.....</td>
<td>1.05 (1.00-1.10)</td>
<td>.04</td>
</tr>
<tr>
<td>On oral medicationf</td>
<td>1.39 (1.00-1.93)</td>
<td>.05</td>
<td>3.47 (1.82-6.60)</td>
<td>&lt;.001</td>
<td>1.22 (0.79-1.89)</td>
<td>.37</td>
</tr>
<tr>
<td>Presence of DR</td>
<td>2.21 (1.52-3.22)</td>
<td>&lt;.001</td>
<td>2.42 (1.63-3.99)</td>
<td>&lt;.001</td>
<td>1.58 (0.99-2.52)</td>
<td>.06</td>
</tr>
<tr>
<td>Previous AAs</td>
<td>0.88 (0.52-1.48)</td>
<td>.62</td>
<td>.....</td>
<td>.....</td>
<td>0.24 (0.14-0.41)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Presence of PSC</td>
<td>1.50 (0.94-2.39)</td>
<td>.01</td>
<td>.....</td>
<td>.....</td>
<td>0.31 (0.14-0.70)</td>
<td>.005</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>0.48 (0.26-0.91)</td>
<td>.02</td>
<td>0.60 (0.31-1.17)</td>
<td>.13</td>
<td>0.47 (0.22-1.00)</td>
<td>.05</td>
</tr>
</tbody>
</table>

Abbreviations: AMI, acute myocardial infarction; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); BP, blood pressure; CI, confidence interval; DR, diabetic retinopathy; ellipses, multivariate analyses not performed owing to insignificant P value in age-sex analysis; HbA1c, glycated hemoglobin; OR, odds ratio; PSC, posterior subcapsular cataract; SES, socioeconomic status (measured by education and income).

aGlycemic control indicates a glycated HbA1c level of 7% or greater; blood pressure, greater than 130/80 mm Hg.

bAdjusted for age and sex.

cNumerals in boldface indicate statistical significance at P < .05.

dAdjusted for age, sex, SES, awareness of diabetes, oral hypoglycemic agent use, presence of DR, total cholesterol, diastolic BP, previous fractures, presence of age-related macular degeneration, and previous stroke.

eAdjusted for age, sex, SES, total cholesterol, BMI, self-reported hypertension, presence of DR, presence of PSC, previous AMI, and previous stroke.

fOral hypoglycemic agents or antihypertensives, as appropriate.

importance of BP control, suggesting that a lack of patient awareness may contribute to the low proportions achieving optimal control. Similarly, an audit of BP control in 100 patients with DR in the United Kingdom found that only 38% of patients achieved BP of 140/80 mm Hg or less despite 70% of patients being treated with antihypertensive medication. In the United Kingdom Prospective Diabetes Study, each 10–mm Hg reduction in systolic BP resulted in a 13% reduction in the development and progression of DR. The ADVANCE Retinal Measurements study showed that in persons with diabetes, even in those without hypertension, BP lowering reduced the occurrence of macular edema. Findings from these studies consistently document the importance of glycemic and BP control and demonstrate a big gap between targeted and achieved optimal control levels.

The prevalence of DR in Asian countries has been increasing dramatically in recent decades and is comparable with that of Western societies. The prevalence of DR in our sample (35.4%) was higher than that found in the Blue Mountains Eye Study (32.4%) and the Barbados Eye Study (28.5%). Another Asian study in rural China, the Handan Eye Study, documented a much higher prevalence of DR (43.1%). Given that DR is associated with a wide range of negative consequences including substantial economic costs, emotional distress, and increased risk of systemic complications (stroke, coronary heart disease, cardiovascular mortality), greater understanding of factors associated with suboptimal control would assist efforts to reduce the burden of DR.

Several factors were found to be associated with suboptimal HbA1c. Individuals with newly diagnosed diabetes (OR, 7.6) who took oral hypoglycemic agents (OR, 3.5) were more likely to have suboptimal HbA1c, highlighting the importance of early detection and the difficulty of achieving optimal glycemic control despite oral medication. Higher total serum cholesterol levels were also associated with suboptimal glycemic control, consistent with previous studies. Similarly, multiple factors were found to be associated with suboptimal BP. In our study, individuals with older age, male sex, higher serum cholesterol levels, higher body mass index, and posterior subcapsular cataract were more likely to have suboptimal BP control, consistent with previous studies. A previous interventional trial demonstrated that weight loss in type 2 diabetes was associated with improved BP control. A first-degree family history of diabetes was associated with lower odds of suboptimal BP, suggesting that likely support from family members diagnosed with diabetes may positively influence patients’ adherence to management guidelines for BP control targets.

Surprisingly, education, income, and socioeconomic status were not found to be associated with poorer control in our study, contrasting previous studies. This could be owing to the large proportion of our sample with low education status and income, and hence a lower statistical power to detect significant differences in glycemic and BP control.

The strengths of our study include its population-based sample, masked external grading of retinal photographs with high proportions of gradable photographs, and standardized measurements of HbA1c and BP. A major limitation was the definition of diabetes used, which was based on random blood glucose levels (and other criteria) instead of oral glucose tolerance tests. In conclusion, our population-based study in this Malay population documented low proportions of persons with diabetes achieving targeted levels of diabetic control, with only 1 in 4 achieving optimal glycemic control.
control and 1 in 8 achieving optimal BP control. Among indi-

viduals with DR, this was even lower. Our findings present a challenge to health care policy-makers and profes-
sionals regarding effective implementation of diabetes care in Asia.

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