Research: Epidemiology

Prevalence of diabetes in Malaysia and usefulness of HbA$_{1c}$ as a diagnostic criterion


$^1$Cardiovascular, Diabetes and Nutrition Research Centre, Institute for Medical Research, Kuala Lumpur, $^2$School of Medicine and Health Sciences, Monash University Malaysia, Kuala Lumpur, $^3$School of Medical Sciences, University Sains Malaysia, $^4$Penang Medical College, Malaysia, $^5$Department of Medicine, Universiti Kebangsaan Malaysia, $^6$Department of Medicine, University of Malaya, and $^7$Department of Medicine, Universiti Malaysia Sabah, Malaysia

Accepted 14 February 2013

Abstract

**Aim** The prevalence of diabetes mellitus among Malaysians aged $\geq$ 30 years of age has increased by more than twofold over a 20-year period. This study aimed to determine the current status and to evaluate the diagnostic usefulness of the HbA$_{1c}$ cut-off point of 48 mmol/mol (6.5%).

**Methods** Using a two-stage stratified sampling design, participants aged $\geq$ 18 years were recruited from five zones selected to represent Malaysia. An oral glucose tolerance test was performed on all those not known to have diabetes.

**Results** A total of 4341 subjects were recruited. By World Health Organization criteria, the prevalence of diabetes mellitus was 22.9%; of that percentage, 10.8% was known diabetes and 12.1% was newly diagnosed diabetes. Diabetes was most prevalent amongst Indians (37.9%) and Malays (23.8%). Prevalence of new diabetes mellitus was only 5.5% (95% CI 4.9–6.3) when based on the HbA$_{1c}$ diagnostic criteria of 48 mmol/mol (6.5%) and, although the cut-off point was highly specific (98.1%), it was less sensitive (36.7%) compared with 45 mmol/mol (6.3%), which showed the optimal sum of sensitivity (42.5%) and specificity (97.4%) in identifying new diabetes mellitus.

**Conclusion** This study recorded an overall diabetes prevalence of 22.6%, almost a twofold increase from 11.6% reported in 2006. This was likely attributable to the higher prevalence of new diabetes (12.1%) diagnosed following an oral glucose tolerance test. An HbA$_{1c}$ of 45 mmol/mol (6.3%) was found to be a better predictive cut-off point for detecting new diabetes in our multi-ethnic population.

Diabet. Med. 00, 000–000 (2013)

Introduction

Most epidemiological reports on diabetes have been based on the World Health Organization (WHO) criteria of diagnosis, utilizing glucose levels at fasting and/or at 2 h following a 75-g oral glucose load (oral glucose tolerance test) [1]. Recently, HbA$_{1c}$ has been endorsed as a new diagnostic tool for diabetes [2]. However, studies have shown that the proposed HbA$_{1c}$ cut-off point of 48 mmol/mol (6.5%), although specific, has lower sensitivity to diagnose diabetes in different populations [3–7].

The prevalence of diabetes among Malaysian adults $\geq$ 30 years of age has increased from 6.3 to 8.3 to 14.9% in 1986, 1996 and 2006, respectively [8–10]. A population-based survey was recently carried out to determine the prevalence of the metabolic syndrome [11] and we report the prevalence of diabetes among the study population based on World Health Organization and HbA$_{1c}$ diagnostic criteria.

Methods

The study utilized a two-stage stratified sampling design. Dividing Malaysia into five zones, one most populous state with an adequate proportion of the major ethnic groups was chosen from each zone as a study site. At each study site, enumeration blocks used by the Department of Statistics Malaysia [12] to divide the country into contiguous geographical areas were then used to randomly select households and, at each selected household, the Kish table for the World Health Survey [13] was used to select one eligible subject ($\geq$ 18 years old) for the study. Ethical approval was obtained from the Medical Research and Ethics Committee, Ministry of Health Malaysia.
Subjects fasted for 10–12 h prior to study visit. An oral glucose tolerance test using 82.5 mg dextrose monohydrate (equivalent to 75 g of anhydrous glucose) in 250 ml of water was performed in all subjects who claimed not to have diabetes at the start of the study. Venous blood was taken for fasting plasma glucose and at 2 h post-oral glucose tolerance test (2-h plasma glucose). All samples were analysed in a central laboratory, using a Selectra XL chemistry analyser (Vital Scientific, Spankeren, the Netherlands) for glucose and an Arkray Adams HA-8160 (Arkray, Inc., Nakagyo-ku, Kyoto, Japan), Diabetes Control and Complications Trial-aligned cation-exchange chromatography analyser for HbA1c.

Data were entered using EpiData Entry 3.1 (EpiData Association, Odense, Denmark) and all statistical analyses were performed using Stata software version 10.1 (Stata Corp., College Station, TX, USA). The status of diabetes was based on personal declaration of having diabetes, by World Health Organization criteria (fasting plasma glucose ≥ 7.0 mmol/l and/or 2-h plasma glucose ≥ 11.1 mmol/l) and by HbA1c-recommended diagnostic criterion. The receiver operating characteristic curve was used to assess and determine the best predictive cut-off points for HbA1c for detecting individuals with new diabetes.

Results

A total of 4341 subjects participated in the study; 470 subjects claimed to have diabetes while 3871 underwent an oral glucose tolerance test. Data from five subjects were omitted in the current analysis because of an incomplete data set. As shown in Table 1, 62.1% of subjects had a normal response to the glucose load, while 37.9% could be categorized as pre-diabetes, with either impaired fasting glucose or impaired glucose tolerance, or both. The overall prevalence of diabetes was 22.9%, where 10.8% was known diabetes and 12.1% was new diabetes. Subjects with known diabetes were found to be significantly older, but all other characteristics, such as BMI, waist circumference and blood pressure, were comparable between the groups (Table 1). Prevalence was comparable between genders and between urban and rural areas. Diabetes was most prevalent among Indians (37.9%) and Malays (23.8%), while pre-diabetes was more prevalent among Indians and Malays, and higher in women (21.9%) and urban dwellers (21.5%). The prevalence of new diabetes was 8.2% (95% CI 7.4–9.1) when diabetes was diagnosed only based on fasting plasma glucose. Among the 525 individuals with new diabetes, 207 (39.4%) had fasting plasma glucose below 7.0 mmol/l and diagnosis was based on a 2-h plasma glucose measurement of ≥ 11.1 mmol/l.

Using the recommended HbA1c cut-off point of 48 mmol/mol (6.5%), prevalence of new diabetes was only 5.5% (95% CI 4.9–6.3). Only 240 (6.2%) of the 3866 subjects who underwent an oral glucose tolerance test had HbA1c above this threshold value. There were 23 (0.6%) individuals without HbA1c results because of interference from haemoglobin variants, as seen on their chromatogram printouts. Of the remaining 3843 individuals, 336 (8.7%) would be misdiagnosed as not having diabetes by HbA1c diagnostic criterion; 170 (50.6%) had fasting plasma glucose ≥ 7.0 mmol/l and the remaining 166 (49.4%) had 2-h plasma glucose in the diabetes range. By receiver operating curve analysis, the HbA1c cut-off point of 48 mmol/mol (6.5%) was found to be

<table>
<thead>
<tr>
<th>Variables</th>
<th>*Normal glucose tolerance (n = 2402)</th>
<th>Known diabetes (n = 470)</th>
<th>*New diabetes (n = 525)</th>
<th>*Pre-diabetes (n = 939)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>44.5 ± 14.5</td>
<td>56.6 ± 11.4</td>
<td>52.7 ± 12.8</td>
<td>50.1 ± 13.5</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.9 ± 4.9</td>
<td>27.4 ± 4.8</td>
<td>28.0 ± 5.6</td>
<td>27.0 ± 5.2</td>
</tr>
<tr>
<td>Waist (cm)</td>
<td>Male 85.8 ± 11.8</td>
<td>93.6 ± 11.5</td>
<td>93.1 ± 13.0</td>
<td>91.5 ± 10.9</td>
</tr>
<tr>
<td></td>
<td>Female 82.6 ± 12.9</td>
<td>90.8 ± 12.0</td>
<td>90.0 ± 12.5</td>
<td>87.4 ± 12.6</td>
</tr>
<tr>
<td>Blood pressure (mmHg)</td>
<td>Systolic 127 ± 20</td>
<td>142 ± 27</td>
<td>141 ± 23</td>
<td>138 ± 23</td>
</tr>
<tr>
<td></td>
<td>Diastolic 76 ± 11</td>
<td>82 ± 11</td>
<td>83 ± 14</td>
<td>81 ± 12</td>
</tr>
<tr>
<td>Overall prevalence</td>
<td>55.4 (53.9–56.9)</td>
<td>10.8 (9.9–11.8)</td>
<td>12.1 (11.2–13.1)</td>
<td>21.7 (20.5–22.9)</td>
</tr>
<tr>
<td>By ethnicity</td>
<td>Malay (n = 2715) 53.6 (51.7–55.5)</td>
<td>11.4 (10.2–12.7)</td>
<td>12.4 (11.2–13.7)</td>
<td>22.6 (21.1–24.2)</td>
</tr>
<tr>
<td></td>
<td>Chinese (n = 632) 59.5 (55.6–63.3)</td>
<td>9.2 (7.2–11.7)</td>
<td>9.2 (7.2–11.7)</td>
<td>22.2 (19.0–25.6)</td>
</tr>
<tr>
<td></td>
<td>Indian (n = 370) 43.2 (38.1–48.5)</td>
<td>21.1 (17.2–25.5)</td>
<td>16.8 (13.3–20.9)</td>
<td>18.9 (15.1–23.3)</td>
</tr>
<tr>
<td></td>
<td>Others (n = 624) 78.0 (74.6–81.2)</td>
<td>4.0 (2.7–5.9)</td>
<td>6.6 (4.8–8.8)</td>
<td>11.4 (9.8–14.1)</td>
</tr>
<tr>
<td>By gender</td>
<td>Male (n = 1523) 59.9 (53.8–55.9)</td>
<td>11.9 (10.4–13.7)</td>
<td>10.3 (8.9–11.9)</td>
<td>17.9 (16.0–19.9)</td>
</tr>
<tr>
<td></td>
<td>Female (n = 2813) 55.8 (53.9–57.8)</td>
<td>10.2 (9.1–11.4)</td>
<td>12.1 (10.9–13.4)</td>
<td>21.9 (20.4–23.5)</td>
</tr>
<tr>
<td>By location</td>
<td>Urban (n = 2213) 55.9 (53.8–58.0)</td>
<td>11.1 (9.8–12.5)</td>
<td>10.2 (9.1–11.4)</td>
<td>21.5 (19.8–23.2)</td>
</tr>
<tr>
<td></td>
<td>Rural (n = 2123) 58.8 (56.5–60.7)</td>
<td>11.9 (10.6–13.4)</td>
<td>11.6 (10.3–13.0)</td>
<td>19.5 (17.8–21.2)</td>
</tr>
</tbody>
</table>

*Defined by World Health Organization criteria.
highly specific (98.1%), but was less sensitive (36.7%) compared with a cut-off point of 45 mmol/mol (6.3%), which showed the optimal sum of sensitivity (42.5%) and specificity (97.4%) in identifying new diabetes based on World Health Organization criteria for diagnosing diabetes.

Among the ethnic groups, Malays showed the highest proportion with diabetes when based on World Health Organization criteria (Fig. 1). However, when diagnostic criteria were based on World Health Organization criteria as well as an HbA1c ≥ 48 mmol/mol (6.5%), the Indians showed the highest proportion with diabetes (11.2%) compared with the Malays (5.2%) and Chinese (2.4%). In all three ethnic groups, only 1–1.4% of the subjects would be diagnosed with diabetes if only the recommended HbA1c ≥ 48 mmol/mol (6.5%) was used.

**Discussion**

This study has shown that, irrespective of the different criteria used, the prevalence of diabetes in Malaysia has increased drastically over the last 2 years, from 11.6% [10] in 2006 to the current overall prevalence of 22.9%, where 12.1% was newly diagnosed. However, the real burden of the disease may have been underestimated as diagnosis in all earlier surveys was based on a single, finger-pricked capillary blood glucose measurement using a glucometer. As shown in this study, there were 3549 individuals classified as not having diabetes if based solely on fasting plasma glucose < 7 mmol/l, but, by performing oral glucose tolerance test, an additional 207 individuals (5.8%) were found to have 2-h plasma glucose ≥ 11.1 mmol/l, suggesting a role for the oral glucose tolerance test in identifying individuals who would otherwise be misdiagnosed if only fasting plasma glucose was measured. However, our current findings were limited to only a single measurement, whereas fasting plasma glucose and 2-h plasma glucose have been known to exhibit high within-person variability [14] and diagnosis ideally should be confirmed by repeat testing on a different day [15].

Another important finding of this study that calls for urgent public health attention was the large number of subjects with pre-diabetes. With a prevalence of 21.7%, and in the absence of immediate and effective interventions, these individuals are at very high risk of developing not only diabetes, but also cardiovascular disease, and all associated complications [16,17].

The prevalence of new diabetes was much lower when the diagnosis was based on the HbA1c cut-off point and up to 336 individuals diagnosed with diabetes by World Health Organization criteria had an HbA1c level below the cut-off point. Other studies have shown that the optimal diagnostic cut-off point for HbA1c varies not only with ethnicity, age and gender, but is also influenced by the prevalence of diabetes in the particular population [18]. As seen in this study, an HbA1c of 48 mmol/mol (6.5%), although highly specific (98.1%), was less sensitive (36.7%) in diagnosing diabetes. Instead, an HbA1c cut-off point of 45 mmol/mol (6.3%) was found to give the maximal sum of sensitivity (42.5%) and specificity (97.4%). This is comparable with the cut-off point proposed by Tavintharan et al. [19], who studied similar multi-ethnic population to ours. Other optimal HbA1c cut-off points recommended for specific ethnicity include between 43 and 46 mmol/mol (6.1–6.4%) for adult Asian Indians [5], between 49 and 53 mmol/mol (6.6–7%) for Singaporean Malays [20] and 38 mmol/mol (5.6%) for the Chinese population of Qingdao, China [21]. A large-scale and long-term follow-up cohort study on normal individuals of different ethnicity would undoubtedly provide better evidence of the diagnostic accuracy of HbA1c at different cut-off levels. Nevertheless, taking into account the inconvenience of 8–10 h of fasting for measuring fasting plasma glucose, or performing the time-consuming oral glucose tolerance test, plus the day-to-day variability in glucose, measuring HbA1c may seemed to be a good alternative diagnostic test for diabetes, especially when screening for diabetes in a large population.

In conclusion, this study has highlighted the alarming increase in the prevalence of diabetes in Malaysia, regardless of the diagnostic criteria used. As a result of urbanization, changing lifestyle and poor dietary habits, geographical location is no longer an important predictor for developing diabetes in Malaysia. This is in contrast with findings reported over 19 years ago, which showed that urban dwellers had a higher prevalence of diabetes compared with people living in a rural setting [22]. The HbA1c threshold of 48 mmol/mol (6.5%) as a diagnostic criterion may underestimate the burden of this disease and a cut-off point of 45 mmol/mol (6.3%) was found to give the maximal sum of sensitivity (42.5%) and specificity (97.4%). In the absence of immediate and effective public health interventions, the current situation is enough to severely paralyse the healthcare system of this country.
Funding sources
This study was supported by a grant from the Ministry of Health Malaysia (06-CAM-02-1).

Competing interests
None declared.

Acknowledgements
We thank the Director General of Health Malaysia for permission to publish this study.

References