The 1997 American Diabetes Association and 1999 World Health Organization Criteria for Hyperglycemia in the Diagnosis and Prediction of Diabetes

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OBJECTIVE — The 1997 American Diabetes Association (ADA) and the 1985 and 1999 World Health Organization (WHO) criteria for diabetes and hyperglycemia differ. The appropriateness of these diagnostic criteria in terms of individuals identified as abnormal and their prognosis has been debated. The purpose of this study is to compare the classifications of people by these criteria and to compare fasting and postload plasma glucose concentrations in the prediction of diabetes.

RESEARCH DESIGN AND METHODS — The frequencies of diabetes by the 3 sets of criteria were compared in 5,023 adult Pima Indians not taking hypoglycemic drugs. Among nondiabetic subjects, fasting plasma glucose (FPG) and 2-h postload plasma glucose (2-h PG) concentrations and categories of impaired glucose regulation or diabetes were evaluated as predictors of diabetes defined by 1999 WHO criteria.

RESULTS — The frequency of diabetes was 12.5% by 1997 ADA criteria, 14.6% by 1985 WHO criteria, and 15.3% by 1999 WHO criteria. The incidence of diabetes was strongly related to higher FPG and 2-h PG, each of which had very similar predictive powers. Impaired glucose tolerance (IGT) was more common than impaired fasting glucose (IFG) (15 vs. 5%), but the 5-year incidence of diabetes was higher in IFG than IGT (37 vs. 24%).

CONCLUSIONS — The prevalence and incidence of diabetes are somewhat lower with the ADA criteria than with the 1985 or 1999 WHO criteria. The intermediate categories of glycemia differ substantially. IFG defines a smaller number of people who are at higher risk of developing diabetes than those with IGT. More people at high risk of diabetes could be identified by using either IFG or IGT, as recommended by the 1999 WHO criteria, or by using the FPG concentration alone, but with a lower cutoff value.

Diabetes Care 23:1108–1112, 2000

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Received for publication 20 January 2000 and accepted in revised form 1 May 2000.

Abbreviations: 2-h PG, 2-h postload plasma glucose; ADA, American Diabetes Association; FPG, fasting plasma glucose; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; OGTT, oral glucose tolerance test; ROC, receiver operator characteristic; WHO, World Health Organization.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.
Table 1—Number of subjects and percentage (%) of the total distribution by fasting and 2-h PG concentrations and WHO and ADA diagnostic groups in 5,023 Pima Indians at baseline

<table>
<thead>
<tr>
<th>FPG (mmol/l)</th>
<th>2-h PG (mmol/l)</th>
<th>Total</th>
<th>n</th>
<th>n (%)</th>
<th>WHO-1985</th>
<th>WHO-1999</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6.1</td>
<td>7.8–11.0</td>
<td>11.1</td>
<td></td>
<td></td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>6.1–6.9</td>
<td>7.8–11.0</td>
<td>11.1</td>
<td></td>
<td></td>
<td>IGT</td>
<td>IGT</td>
</tr>
<tr>
<td>7.0–7.7</td>
<td>7.8–11.0</td>
<td>11.1</td>
<td></td>
<td></td>
<td>Diabetes</td>
<td>Diabetes</td>
</tr>
<tr>
<td>≥7.8</td>
<td>7.8–11.0</td>
<td>11.1</td>
<td></td>
<td></td>
<td>ADA</td>
<td>ADA</td>
</tr>
</tbody>
</table>


WHO criteria (5–7). In 1999, the WHO made further recommendations regarding criteria for diagnosis of diabetes and other categories of impaired glucose regulation (8). They incorporate the change in the FPG diagnostic level to ≥7.0 mmol/l but retain the recommendation for the OGTT and diagnosis of diabetes if the 2-h PG is ≥11.1 mmol/l.

In this article, the characteristics of the 3 sets of criteria (ADA, and 1985 and 1999 WHO) are compared using longitudinal data on fasting and 2-h PG concentrations from the Pima Indian population. FPG and 2-h PG are compared as predictors of diabetes defined by each set of criteria.

RESEARCH DESIGN AND METHODS

Subjects and measures

A longitudinal study of diabetes and its complications in Pima Indian residents of the Gila River Indian Community in Arizona has been conducted since 1965 (9). Every 2 years, all residents of a defined area of the community aged ≥5 years are invited to participate in a standardized medical examination including a medical history and physical examination. At each examination, an OGTT is performed with determination of venous plasma glucose, fasting and 2 h after the ingestion of 75 g glucose. Data are presented from examinations, an OGTT is performed with determination of venous plasma glucose, fasting and 2 h after the ingestion of 75 g glucose. Data are presented from examinations of people ≥15 years of age conducted since 1975, when routine testing of participants in the fasting state began.

The following diagnostic criteria for diabetes were used:

- ADA criteria: FPG ≥7.0 mmol/l (i.e., the criterion recommended for determining the prevalence and incidence of the disease);
- 1985 WHO criteria: FPG ≥7.8 mmol/l or 2-h PG ≥11.1 mmol/l; and
- 1999 WHO criteria: FPG ≥7.0 mmol/l or 2-h PG ≥11.1 mmol/l.

Although clinical diagnosis requires a confirmatory test, in this article, these classifications were made, as in epidemiologic studies, on the basis of single examinations. Note that anyone meeting either of the first 2 criteria for diabetes also meets the 1999 WHO criterion.

Among people determined nondiabetic by each criterion, impaired glucose tolerance (IGT) is defined by 2-h PG ≥7.8 to <11.1 mmol/l, and in the ADA and 1999 WHO criteria, impaired fasting glucose or glycemia (IFG) is defined by FPG ≥6.1 to <7.0 mmol/l.

Statistical analysis

Prevalence of diabetes. At the first examination at which FPG and 2-h PG were measured, the presence of diabetes diagnosed by the ADA or the 1985 or 1999 WHO criteria was determined among subjects not taking oral hypoglycemic agents or insulin.

Incidence of diabetes. Incidence rates of diabetes by the ADA or the 1985 or 1999 WHO criteria were calculated in longitudinal data from people who at baseline were nondiabetic by the criterion in question. Individuals taking oral hypoglycemic agents or insulin during follow-up were considered to have diabetes by each of these criteria. Incidence rates were expressed as the number of patients divided by person-years from baseline until the development of diabetes or until the last examination (9). The 5-year cumulative incidence of diabetes was calculated by the Kaplan-Meier method (10). For simplicity, most of the results of incidence calculations are shown only for diabetes defined by the 1999 WHO criteria, since this set of criteria is the most recent and is the same as the ADA criteria if the 2-h PG result is included.

Sensitivity and specificity for predicting diabetes. The ability of FPG or 2-h PG to predict the development of diabetes by 1999 WHO criteria at the first follow-up examination was determined by computing sensitivity and specificity and plotting them in a receiver operating characteristic (ROC) curve (11). Among 2,743 people
determined nondiabetic by 1999 WHO criteria at baseline and with a follow-up examination, the sensitivity for a given cut-point value was computed as the number with a baseline glucose of at least that cut-point value divided by the number with diabetes at follow-up. The specificity was the number with baseline glucose below the cut-point value divided by the number remaining nondiabetic. The sensitivity and specificity were computed over a wide range of FPG values and, for comparison, with selected values of 2-h PG or FPG combined with 2-h PG. The area under an ROC curve represents the probability that a subject chosen at random from the group who developed the outcome of interest had a higher test value than one from those who did not.

RESULTS

Prevalence of diabetes
The distribution of the 5,023 subjects by glucose concentrations and their classifications according to the 3 sets of criteria are shown in Tables 1 and 2. For 97.5% of the subjects, the WHO-1985 and WHO-1999 classifications were the same. They differed only in the 93 nondiabetic subjects who met the 1999 definition of IFG and the 35 (14 + 21) who were diabetic by having FPG 7.0–7.7 mmol/l and 2-h PG <11.1 mmol/l. The prevalence of diabetes was 14.6% by the 1985 or 15.3% by the 1999 WHO criteria. By contrast, 629 people (12.5%) had diabetes by the ADA criteria (FPG ≥7.0 mmol/l). This was fewer than the 768 diabetic by the 1999 WHO criteria because of the 139 people (60 + 79) with 2-h PG ≥11.1 mmol/l but FPG <7.0 mmol/l. Thus, among the 768 subjects with diabetes by the 1999 WHO criterion, 82% met the ADA criteria and 95% met the 1985 WHO criteria.

Incidence of diabetes
The incidence of diabetes by each criterion was determined among those not diabetic by the corresponding criterion at baseline. There were 678 new cases of diabetes diagnosed by ADA criteria in 27,586 person-years of follow-up, 749 new cases of diabetes diagnosed by 1985 WHO criteria in 26,743 person-years, and 767 new cases of diabetes diagnosed by 1999 WHO criteria in 26,386 person-years of follow-up. By the ADA criteria, the incidence of diabetes was 12% lower than by the 1985 WHO criteria and 15% lower than by the 1999 WHO criteria.

In Figure 1, the incidence rate of diabetes by 1999 WHO criteria according to baseline FPG and 2-h PG distributions is shown. The curves for FPG and 2-h PG were nearly indistinguishable.

In Figure 2, the cumulative incidence of diabetes by 1999 WHO criteria is shown for normal fasting and 2-h PG, IFG, and IGT.

Figure 1—The incidence rate of diabetes by 1999 WHO criteria according to baseline FPG and 2-h PG. FPG and 2-h PG distributions are divided from low to high (1–20) in 5th-percentile intervals.

Figure 2—The cumulative incidence of diabetes by normal fasting and 2-h PG, IFG, and IGT.
includes a smaller, but more extreme, part of the glucose distribution.

Among subjects with normal FPG and 2-h PG, IGT alone (FPG < 6.1 mmol/l and 2-h PG 7.8–11.0 mmol/l), IFG alone (FPG 6.1–6.9 mmol/l and 2-h PG < 7.8 mmol/l), or both IFG and IGT (FPG 6.1–6.9 and 2-h PG = 7.8–11.0 mmol/l), the 5-year cumulative incidences of diabetes were 3.6, 19.9, 31.0, and 41.2%, respectively. Thus, IFG defines a higher risk category than IGT. Nevertheless, individuals with IGT but not IFG had a cumulative incidence of diabetes 5.5 times as high as those with "normal" FPG and 2-h PG.

Sensitivity and 1 — specificity of FPG for predicting diabetes by 1999 WHO criteria are plotted as an ROC curve in Fig. 3. Points representing the FPG values of 5.7 and 6.1 mmol/l are indicated along with the percentage of the baseline population with values at or above these points in parentheses. FPG ≥ 5.7 mmol/l, defining a group representing the same percentage of the population (15%) as IGT (Fig. 2), has sensitivity and specificity almost identical to those of IGT, as indicated in Fig. 3 by the point for 2-h PG ≥ 7.8 mmol/l. IFG (FPG ≥ 6.1 mmol/l) is much less common (5%), and as a result, its sensitivity for prediction of diabetes is lower, but its specificity is higher. The 2 triangles on the curve represent 2-h PG ≥ 7.8 and ≥ 9.3 mmol/l. These cutoff points define parts of the baseline population including the same percentages as the FPG values of ≥ 5.7 and ≥ 6.1 mmol/l. The area under the ROC curve for predicting diabetes is lower, but its specificity is almost identical to the corresponding FPG values. The category impaired glucose regulation (IGF or IGT, i.e., FPG ≥ 6.1 mmol/l or 2-h PG ≥ 7.8 mmol/l) includes substantially fewer people than the category of IGT. The 5-year cumulative incidence of diabetes is lower in IGT than IFG, but more people at risk are identified when IGT is used. If categories of FPG and 2-h PG are defined to include similar percentages of their respective distributions, their predictive values for diabetes are equivalent. The difference in IGT and IFG reflects the fact that they represent different proportions of the glucose distributions rather than that FPG or 2-h PG per se are inherently different in their sensitivity, specificity, or predictive value. Among the Pima Indians, the FPG cutoff point of ≥ 5.7 mmol/l had similar sensitivity and positive predictive value as IGT for predicting subsequent diabetes, although the choice of such a cutoff point might differ among populations. It is, therefore, not necessary to perform an OGTT to obtain the same sensitivity for predicting future diabetes as is obtained by IGT; this can be accomplished simply by using a lower level of FPG.

When it is feasible to perform glucose tolerance testing, the combination of FPG and 2-h PG provides somewhat more information than either alone. In practice, however, glucose tolerance testing is not usually performed unless diabetes is suspected. Measurement of FPG alone provides considerable information, and its widespread use could identify many more people who could benefit from intervention.

Diagnostic criteria cannot be based only on comparison of the resultant prevalence and incidence rates of the disease, but should also be based on their abilities to predict specific complications of diabetes (12) and other serious outcomes, such as
ADA and WHO criteria and the prediction of diabetes

cardiovascular disease (13,14) or mortality. Differences in outcome according to the different diagnostic criteria are examined in a companion article (15).

In summary, most Pima Indians with diabetes by either the 1985 or 1999 WHO or the ADA criteria met all 3 criteria simultaneously. The prevalence of intermediate categories of glycemia differed, however, with the ADA category of IFG defining a smaller proportion of the population who are at higher risk of developing diabetes than those with IGT. Using a cutoff FPG level lower than that currently used to define IFG could identify a greater proportion of the population at high risk of diabetes but at the cost of lower specificity and predictive value.

Acknowledgments — We thank the members of the Gila River Indian Community for participating in this research and the staff of the Diabetes and Arthritis Epidemiology Section, National Institute of Diabetes and Digestive and Kidney Diseases, for conducting the examinations.

References