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ORIGINAL ARTICLE

Prevalence of Diabetes in Asian Indians Based on Glycated Hemoglobin and Fasting and 2-H Post-Load (75-g) Plasma Glucose (CURES-120)

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Abstract

Objective: With the introduction of glycated hemoglobin (A1c) as a method of screening for diabetes, it is essential to study how use of A1c would affect the prevalence of diabetes in different ethnic groups. We compared the prevalence of diabetes by fasting (FPG) and 2-h post-load (75-g) plasma glucose (2-h PG) and A1c criteria in an Asian Indian population.
Research Design and Methods: Subjects ($n = 2,188$) without known diabetes were drawn from the Chennai Urban Rural Epidemiological Study, a population-based study in Chennai, South India. FPG, 2-h PG, and A1c estimations were carried out. Prevalence rates of diabetes were compared using as cut points FPG ≥7 mmol/L (126 mg/dL), 2-hr PG ≥11.1 mmol/L (200 mg/dL), or A1c ≥6.5% criteria.
Results: Prevalence of diabetes was 6.1% ($n = 134$) using the FPG criterion, 10.1% ($n = 221$) by the 2-h PG criterion, and 12.8% ($n = 281$) by the A1c criterion. Thus the prevalence of diabetes by the A1c criterion was 110% and 27% higher than the FPG and 2-hr PG criteria, respectively. Only 121 of these subjects were identified by all three criteria. Subjects diagnosed by the A1c criteria had the lowest FPG, 2-h PG, A1c, and serum triglyceride levels.
Conclusions: In Asian Indians, use of A1c criteria would result in markedly higher prevalence rates of diabetes. It also identifies a different set of individuals with milder glucose intolerance and lower serum triglyceride levels.

Introduction

The criteria of 2-h post-load (75-g) plasma glucose (2-h PG) ≥11.1 mmol/L (≥200 mg/dL)[1] and fasting plasma glucose (FPG) ≥7.0 mmol/L (≥126 mg/dL) have been widely used for detecting diabetes.[2] In 1997, the American Diabetes Association proposed the FPG criterion of ≥7.0 mmol/L (≥126 mg/dL) for detecting diabetes.[2] In 2010, an international expert committee recommended the use of a glycated hemoglobin (A1c) value of ≥6.5% for diagnosis of diabetes.[3,4] A recent World Health Organization Consultation also recommended that A1c ≥6.5% could be used as a cut point for diagnosing diabetes, while it recognizes that a value <6.5% does not exclude diabetes diagnosed using the 2-h PG criterion.[5]

According to the recent Diabetes Atlas published by the International Diabetes Federation, globally there are 366 million people with diabetes.[6] The number projected for India was 61.3 million people with diabetes.[6] The recent Indian Council of Medical Research–India Diabetes (ICMR-INDIAB) study confirmed that there are 62.4 million people with diabetes in India.[7] These figures were based on the 2-h PG criterion. No epidemiological study has compared A1c with 2-h PG or FPG in assessing prevalence of diabetes in Asian Indians. This study reports on the prevalence of diabetes using the three criteria in a population-based study carried out in South India.

Research Design and Methods

The Chennai Urban Rural Epidemiological Study (CURES) is a large cross-sectional study done on a representative population of the metropolitan city of Chennai (formerly Madras) in southern India. The detailed study design of CURES is described elsewhere.[8]

In brief, CURES was carried out in different phases. In Phase 1, 46 of the 155 wards in Chennai were randomly selected for sampling, providing a total sample size of 26,001 individuals ≥20 years old. Phase 2 of CURES dealt with prevalence of diabetes-related complications. In Phase 3, every 10th subject recruited in Phase 1 ($n = 2,600$) was invited for detailed testing including oral glucose tolerance test, maintaining the representativeness of the sample, and the response rate was 90.4% (2,350 of 2,600 participants). For this

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study, we excluded subjects with known diabetes. In all others FPG and 2-h (75-g oral glucose) PG (glucose oxidase–peroxidase method) were measured using a Hitachi-912 autoanalyzer (Hitachi, Mannheim, Germany). A1c was measured using the Variant™ machine (Bio-Rad Laboratories, Hercules, CA), and the coefficient of variation was 3.5%. This method is standardized to the National Glycosylated Hemoglobin Standardization Program. Our laboratory also participates in the Unity Program of Bio-Rad A1c standardization and is certified by the College of American Pathologists.

Statistical analyses were performed using SPSS for Windows version 15.0 software (SPSS Inc., Chicago, IL). Frequency tables were used to explore the performances of A1c, 2-h PG, and FPG in identifying diabetes. One-way analysis of variance (with the Tukey's honestly significant difference) was used to compare groups for continuous variables, and the χ^2 test was used to compare proportions. A P value of <0.05 was considered significant.

Results

Of the total of 2,350 subjects in Phase 3 of CURES, we excluded 143 known diabetes subjects as they were on treatment and therefore not suitable for this study. Of the remaining 2,207 subjects, after excluding subjects who did not undergo A1c testing ($n=19$), 2,188 (response rate, 99.1%) participated. The mean age of participants was 38.7 ± 12.6 years, the mean body mass index was $22.7\,kg/m^2$, and 46% were male.

Figure 1 shows that the prevalence and number of individuals with diabetes were 6.1% ($n=134$), 10.1% ($n=221$), and 12.8% ($n=281$) according to the FPG, 2-h PG, and A1c criteria, respectively.

Table 1 compares the clinical and biochemical features of the subjects diagnosed with diabetes using the three criteria. A1c-diagnosed subjects had significantly lower mean FPG ($P<0.001$), 2-h PG ($P<0.001$), A1c ($P<0.001$), and serum triglycerides ($P=0.015$) compared with individuals diagnosed by the FPG and 2-h PG criteria.

Conclusions

This study makes the following points:

1. The prevalence of diabetes diagnosed by the A1c criterion is highest, followed by the 2-h PG criterion and lowest by the FPG criterion.
2. The A1c criterion identifies a different set of individuals than those diagnosed by 2-h PG and FPG criteria.
3. Those identified by the A1c criterion appear to have milder glucose intolerance and lower serum triglyceride levels.

We report that if the A1c criterion was used to screen for diabetes, prevalence rates would be 110% and 27% higher than that diagnosed by the FPG and 2-h PG criteria, respectively. This would mean that in India the number of people with diabetes would go up from the present 62.4 million as determined by 2-h PG criterion[7] to 79.2 million people with

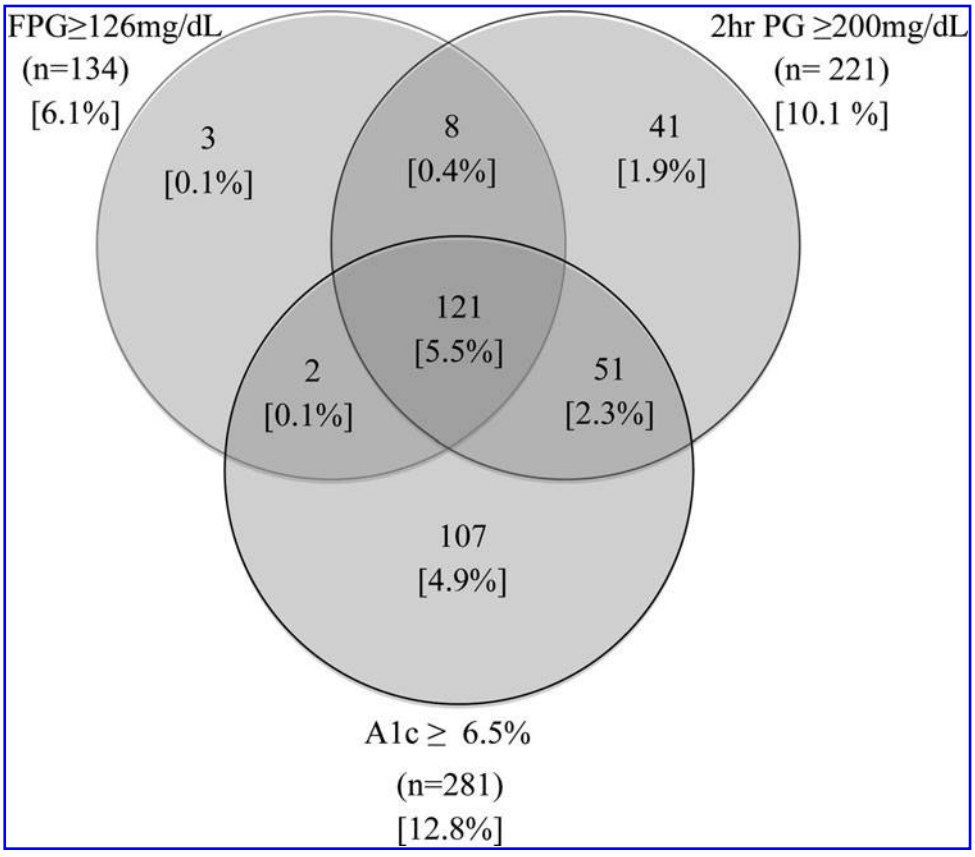

FIG. 1. Venn diagram showing the prevalence of diabetes using the fasting plasma glucose (FPG), 2-h post-load (75-g) plasma glucose (PG), and glycated hemoglobin (A1c) criteria.

Table 1. Clinical and Biochemical Characteristics of Subjects Diagnosed by the Three Criteria

Parameter	*FPG ≥ 126 mg/dL* (n = *134*)	*2-h PG ≥ 200 mg/dL* (n = *221*)	*HbA1c ≥ 6.5%* (n = *281*)	P *value*
Age (years)	43.9 ± 10.6	45.1 ± 12.0	46.1 ± 12.2	0.163
Males [*n* (%)]	76 (56.7%)	111 (50.2%)	146 (52.0%)	
BMI (kg/m^2)	24.2 ± 3.3	24.3 ± 3.1	24.4 ± 3.6	0.822
Waist (cm)	88.1 ± 9.0	88.5 ± 9.1	88.8 ± 9.6	0.802
Blood pressure (mm Hg)				
Systolic	128 ± 20	128 ± 21	127 ± 20	0.826
Diastolic	80 ± 12	79 ± 12	79 ± 12	0.400
FPG (mg/dL)	191 ± 54	155 ± 61	140 ± 59	< 0.001[a]
2-h PG (mg/dL)	316 ± 77	285 ± 73	235 ± 101	< 0.001[a]
A1c (%)	9.3 ± 1.9	8.4 ± 2.0	8.2 ± 1.8	< 0.001[a]
Total cholesterol (mg/dL)	199 ± 41	196 ± 38	197 ± 40	0.877
LDL-C (mg/dL)	119 ± 37	120 ± 35	122 ± 35	0.554
HDL-C (mg/dL)	40 ± 8	40 ± 8	40 ± 8	0.518
Serum triglycerides (mg/dL)[b]	170 ± 2	155 ± 2	145 ± 2	0.015[a]

[a]$P < 0.05$ considered significant.
[b]Data are expressed as geometric mean.
A1c, glycated hemoglobin; BMI, body mass index; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; PG, post-load (75-g) plasma glucose.

diabetes if the A1c criterion was used. The Danish Inter99 Study[9] also showed that the A1c cutoff of 6.5% increased the prevalence of diabetes by 60% compared with the use of the oral glucose tolerance test. Higher prevalence rates of diabetes could have huge economic implications, as the cost of health care would dramatically increase. Moreover, a group of individuals who are currently considered not to have diabetes by 2-h PG and FPG criteria would be classified as having diabetes. This may have some benefits in identifying individuals at an earlier stage in the natural history of the disease. However, as an A1c criterion identifies individuals with lower plasma glucose and serum triglyceride levels, it likely identifies individuals at lower cardiometabolic risk, and the cost-effectiveness of this remains to be established.

Undoubtedly, use of A1c has several advantages. Its testing can be performed at any time of the day and does not require any special preparation such as fasting.[10] However, in developing countries, there are several limitations of using A1c for mass screening. These include lack of standardization of the test and interference by hemoglobinopathies such as sickle cell anemia, thalassemia, or iron deficiency anemia.[11]

The cost of the A1c test also presents a formidable challenge in developing countries. In India, an A1c test currently costs between 250 to 750 Indian rupees (INR) (USD 5–15 per test). The cost of a plasma glucose test is between INR 25 and 75 (USD 0.5–1.5). In the present study the total estimated cost of screening all the participants ($n = 2{,}188$) even using the minimum price for A1c testing (INR 250) would be approximately INR 547,000 (USD 10,940), whereas that of doing an FPG or 2-h PG using a median cost of INR 50 would be INR 109,400 (USD 2,188), a saving of almost 80%. If A1c were used for screening, the cost of detecting one new case of diabetes would be approximately INR 2,000 (USD 40). Using 2-h PG, it would be about INR 500 (USD 10), whereas using FPG it would be INR 820 (USD 16). This is a serious limitation to use of A1c as a screening test for diabetes in developing countries like India. However, in projecting such costs one must always keep in mind the costs of treatment of diabetes and especially its complications, which are much higher.[12] The Screening India's Twin Epidemic study showed a substantial burden of diabetes and hypertension in India and pointed out the need for accurate diagnosis of diabetes.[13] An accompanying editorial in the same issue of the journal also stressed on the rising costs associated with increasing morbidity and mortality due to diabetes and hypertension in India.[14]

The strengths of this study are that it is population-based and is done in an Asian Indian population, which has a high susceptibility for type 2 diabetes. Another advantage is the high response rate. One limitation of our study is that because it is cross-sectional, we cannot compare the ability of A1c and 2-h PG and FPG criteria to predict development of future diabetes in those who are currently normal or the impact of micro- and macrovascular complications in those detected to have diabetes by the three criteria.

In conclusion, in Asian Indians, compared with FPG or 2-h PG, the A1c test provides much higher prevalence rates of diabetes and identifies a different set of individuals, but the test is also far more expensive to screen for diabetes in epidemiological settings.

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Author Disclosure Statement

No competing financial interests exist.

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