

# Diagnostic Testing for Diabetes Using HbA<sub>1c</sub> in the Abu Dhabi Population

## Weqaya: the Abu Dhabi Cardiovascular Screening Program

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**OBJECTIVE**—The validity of HbA<sub>1c</sub> as a population diagnostic tool was tested against oral glucose tolerance testing in Abu Dhabi nationals.

**RESEARCH DESIGN AND METHODS**—The screening tool of HbA<sub>1c</sub> and random glucose was validated against the “gold standard” oral glucose tolerance test according to World Health Organization criteria.

**RESULTS**—The HbA<sub>1c</sub> threshold of 6.4% provided the optimum balance between sensitivity (72.0%) and specificity (84.3%) with positive and negative predictive values of 47.9 and 93.7% and area under the receiver operating characteristics curve of 0.78. This threshold compares with a threshold of 6.5% recommended by the International Scientific Committee and American Diabetes Association and of 6.3% in a recent study in China.

**CONCLUSIONS**—This study successfully validates the feasibility and threshold of HbA<sub>1c</sub> for diagnosis of diabetes at the population level in a Middle-Eastern population. This result is a major step in the fight to tackle the increasing burden of diabetes in the United Arab Emirates.

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The United Arab Emirates (UAE) has been reported as having the second highest world prevalence of diabetes by the World Health Organization (2005) (1) and the International Diabetes Federation (2). The Weqaya program screened >92% of the UAE national population for cardiovascular disease risk factors including diabetes (3). The International Expert Committee on Diabetes (4) and the American Diabetes Association (5) recommended that an HbA<sub>1c</sub> threshold of 6.5% should be diagnostic of diabetes. This article seeks to determine the utility of HbA<sub>1c</sub> as a population-level diagnostic tool.

### RESEARCH DESIGN AND METHODS

The Weqaya screening program commenced in April 2008 for UAE nationals (aged ≥18 years) residing in Abu Dhabi linked to the provision of free comprehensive health insurance (called

Thiqa) (3). Individuals consented in line with the principles of the Abu Dhabi Medical Research Council (6). Further details about the screening program are described elsewhere (3), but in summary, it was conducted at a series of dedicated primary health care facilities with a systematic screening methodology (available at <http://www.haad.ae/HAAD/LinkClick.aspx?fileticket=sj-gI8-BIv4%3d&tabid=820>). Screening recorded demographics and self-reported indicators; anthropometric measures included waist-to-hip ratio, BMI, and a single-arterial blood pressure reading; and blood testing included nonfasting samples for glucose, LDL and HDL cholesterol, and HbA<sub>1c</sub>.

Patients at higher risk of having diabetes (HbA<sub>1c</sub> ≥6.1% or random glucose ≥11.1 mmol/L) or missing HbA<sub>1c</sub> and glucose data from the first round of screening were invited back for further investigation. Fasting glucose levels (12 h fasting), oral

glucose tolerance test (OGTT) using a 75-g glucose load in line with World Health Organization guidelines (7), and HbA<sub>1c</sub> levels were recorded at follow-up. Only individuals attending public facilities were included to ensure standardized laboratory methods. HbA<sub>1c</sub> was measured on whole blood using the Cobas Integra Instrument in line with the National Glycohemoglobin Standardization Program, standardized to the Diabetes Control and Complications Trial reference assay (8).

### Statistical analysis

All statistical analyses were conducted using STATA version 10.0 (STATA Corp LP, College Station, TX). Continuous variables were compared using *t* tests for comparison of means. The screening test was HbA<sub>1c</sub> (ranging from 6.1 to 7%) and random glucose (≥11.1 mmol/L). The reference test was fasting and 2-h glucose after a 75-g glucose load. Diagnostic testing determined sensitivity, specificity, positive predictive value, and negative predictive value. The receiver operating characteristic (ROC) curve areas were determined to compare area under the curve (AUC) for sensitivity versus 1 – specificity.

**RESULTS**—A total of 1,028 subjects were included in this analysis. Mean (95% CI) for BMI and waist circumference were 30.4 kg/m<sup>2</sup> (29.9–30.9) and 97 cm (95.8–98.1). Means for systolic blood pressure and diastolic blood pressure, LDL and HDL cholesterol, triglyceride, and fasting and 2-h postload glucose levels were within normal ranges.

HbA<sub>1c</sub> was diagnostic of diabetes using the American Diabetes Association criteria in 216 (21.0%) of the study sample.

Table 1 shows the sensitivity, specificity, positive predictive value, negative predictive value, and AUC for various thresholds of HbA<sub>1c</sub> against OGTT as the reference test. The results show that the HbA<sub>1c</sub> threshold of 6.4% had the highest AUC of 0.78 (95% CI 0.75–0.82) with sensitivity of 72% (65–78%) and specificity of 84% (82–87%). Using an HbA<sub>1c</sub> threshold of 6.4% to diagnose diabetes would have resulted in 72% of patients

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**Table 1—Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and area under the receiver operating characteristics curve comparing various thresholds of HbA<sub>1c</sub> with the WHO criteria for diabetes**

HbA <sub>1c</sub> level*	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Area under receiver operating characteristic curve†
6.1	82.5 (76.4–87.7)	66.2 (62.9–69.4)	42.8 (40–45.6)	92.5 (90–94.4)	0.74 (0.71–0.78)
6.2	79.9 (73.5–85.4)	73.3 (70.1–76.2)	43.7 (40.4–47)	93.4 (91.3–94.9)	0.77 (0.73–0.80)
6.3	76.7 (70–82.5)	78.2 (75.2–80.9)	44.1 (40.4–47.9)	93.7 (92–95.1)	0.77 (0.74–0.81)
6.4‡	72.0 (65.0–78.2)	84.3 (81.6–86.7)	47.9 (43.4–52.4)	93.7 (92.2–95)	0.78 (0.75–0.82)
6.5	65.6 (58.4–72.4)	89.1 (86.8–91.1)	52.3 (46.8–57.7)	93.4 (92.1–94.5)	0.77 (0.74–0.81)
6.6	61.9 (54.6–68.9)	93 (91.1–94.7)	59.6 (52.9–65.9)	93.7 (92.5–94.7)	0.77 (0.74–0.81)
7.0	40.2 (33.2–47.6)	98.7 (97.7–99.3)	80.7 (69.3–88.5)	92.3 (91.5–93.1)	0.69 (0.66–0.73)

Data in parentheses are 95% CIs. The following criteria were used: fasting glucose  $\geq 7.0$  mmol/L or 2-h glucose (post-75-g glucose load)  $\geq 11.1$  mmol/L, \*plus random glucose level  $\geq 11.1$  mmol/L. †(Sensitivity + specificity)/2. ‡Highest AUC seen for HbA<sub>1c</sub> of 6.4%.

with diabetes being correctly diagnosed and 16% being incorrectly diagnosed.

A comparison of the study cohort with the full Weqaya cohort found higher mean age in this study at 42 years compared with 35 years ( $P < 0.001$ ). Nondiabetic patients in this cohort had higher mean age, BMI, waist circumference, systolic blood pressure, diastolic blood pressure, and LDL cholesterol than nondiabetic patients from the Weqaya cohort. For diabetic patients, mean age and systolic blood pressure were lower in this cohort than in diabetic patients in the Weqaya cohort.

**CONCLUSIONS**—This is one of the first studies to demonstrate the utility of HbA<sub>1c</sub> for diagnosing diabetes and has shown that 6.4% is an optimum HbA<sub>1c</sub> threshold for the Abu Dhabi national population.

#### Use of HbA<sub>1c</sub> as a diagnostic tool

Studies repeatedly demonstrate that within populations, over one-third of all patients with diabetes remain undiagnosed, with resulting complications due to late diagnosis (9). The availability of a single nonfasting blood test could facilitate successful population-level screening programs. The Weqaya study demonstrated this.

HbA<sub>1c</sub> is an independent predictor of cardiovascular events in patients with diabetes and nondiabetic subjects (10), which makes HbA<sub>1c</sub> data from screening programs a valuable resource for public health planning.

#### Comparison with other studies

In this study, an HbA<sub>1c</sub> threshold of 6.4% yielded the highest AUC (0.78). A recent study in China comparing HbA<sub>1c</sub> screening with OGTT demonstrated sensitivity, specificity, and AUC of 63%, 96%, and 0.86, respectively (11). Sensitivities and

specificities reported using fasting plasma glucose as the reference in the Chinese study were 56 and 97% for their optimum HbA<sub>1c</sub> threshold of 6.4% (11) and in National Health and Nutrition Examination Survey data were 59 and 97% for their optimum HbA<sub>1c</sub> threshold of 5.8% (12).

The higher sensitivity and lower specificity in the Weqaya study may be due to population factors affecting glycation of hemoglobin, such as hemoglobinopathies and other abnormal hemoglobin types, anemias (13), vitamins C and E, iron deficiency, and some medication use (14). Different ethnic groups have also been shown to have HbA<sub>1c</sub> levels up to 0.4–0.7% higher than Caucasian populations despite similar glucose levels (15).

#### Choice of HbA<sub>1c</sub> threshold

The choice of HbA<sub>1c</sub> threshold for clinical practice will depend on whether the tool is being used for screening or diagnosis. Screening tests usually warrant the choice of high sensitivity over specificity. Because HbA<sub>1c</sub> has now been recommended for use as a diagnostic test, specificity is increasingly important, and the threshold of 6.4% in this study provides a high specificity without too much compromise of sensitivity.

#### Strength and limitations

This study is the first in a Middle Eastern population to screen at population level using HbA<sub>1c</sub> and has been shown to be representative (3); however, some differences were shown in nondiabetic subjects between this study sample and the overall Weqaya population.

#### Summary

HbA<sub>1c</sub> has been validated as a suitable test for the definitive diagnosis of diabetes in the Weqaya population screening program

in a high-risk Middle-Eastern population. This is a major step in the fight to tackle the increasing burden of diabetes in the UAE.

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C.H. designed the study, conducted data analysis and interpretation, and wrote the manuscript. O.H. and Z.A.S. contributed to the study design and review of the manuscript.

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