

Incidence of type 2 diabetes by HbA_{1c} and OGTT: the Isfahan Diabetes Prevention Study

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Abstract The aim of this study was to estimate the incidence of type 2 diabetes using newly proposed hemoglobin A_{1c} (HbA_{1c}) and current oral glucose tolerance test (OGTT) definition in an Iranian non-diabetic population. A total of 923 non-diabetic first-degree relatives (FDRs) of patients with type 2 diabetes 30–70 years old in 2003–2005 were followed through 2009 for the occurrence of type 2 diabetes. At baseline and through follow-ups, participants underwent a standard 75 g 2-h OGTT and HbA_{1c} measurements. Prediction of progression to type 2 diabetes by OGTT-defined or HbA_{1c}-defined diabetes was assessed with area under the receiver operating characteristic (ROC) curves based upon measurement of fasting plasma glucose, 2-h post-load glucose values, and HbA_{1c}. The prevalence of type 2 diabetes was 9.2% (95% CI: 8.2, 10.2) by OGTT-defined diabetes and 7.9% (95% CI: 6.9, 9.0) by HbA_{1c} ≥ 6.5 . The incidence of type 2 diabetes was 2.0% (95% CI: 1.6, 2.4) (1.8% men and 2.1% women) per year by the current OGTT definition, whereas the incidence rates were 1.7% (95% CI: 1.3, 2.0) (1.6% men and 1.7% women) per year by HbA_{1c} ≥ 6.5 %. Of those diagnosed with type 2 diabetes by OGTT, 69.6% had HbA_{1c} < 6.5 % and therefore would not have been classified as having type 2 diabetes. The incidence and prevalence of diabetes using newly proposed HbA_{1c} threshold in this FDRs of patients with

type 2 diabetes were slightly lower than using current OGTT definition.

Keywords Type 2 diabetes · First-degree relatives · Diagnostic test · HbA_{1c} · Glucose tolerance test

Introduction

The most widely used diagnostic and/or screening test for the detection of diabetes includes fasting plasma glucose (FPG) and the oral glucose tolerance test (OGTT). FPG is a more commonly used test, compared with OGTT, due to its logistical advantages. Hemoglobin A_{1c} (HbA_{1c}) has been suggested as an alternative screening test for type 2 diabetes [1, 2]. However, the significance of HbA_{1c} in identifying persons with a future risk of diabetes remains unknown [3, 4]. The question then arises whether FPG is a better predictor of diabetes risk than post-load glucose values or HbA_{1c}. Although measuring FPG is less expensive, more convenient, and more reproducible than performing an OGTT, various studies have shown that FPG has a sensitivity of only 40–60% for detecting patients with type 2 diabetes [4–7]. In contrast, the OGTT has been the preferred test for diagnosing diabetes in epidemiological studies for over 40 years, despite the widely recognized costs and inconvenience of the test, and has poor reproducibility. In addition, OGTT is time-consuming and shows considerable intra-individual variation, with up to 20% of OGTT-diagnosed patients reclassified as not having diabetes when retested [8–10]. Use of HbA_{1c} has some logistical advantages over both the FPG and the OGTT. It can be measured at any time of day with a small sample of blood and is convenient and easy to do [8]. The disadvantages are the difficulty in standardization and the fact

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that HbA_{1c} cannot be measured in the presence of certain form of anemia and hemoglobin variants [11], which may also have unique ethnic or geographic distributions.

Although concerns about the standardization of assay have largely been resolved in developed world [12], the standardization difficulty still exists in some regions of developing world. The limited access to standardized laboratory HbA_{1c} methods makes unfeasible the inclusion of the HbA_{1c} criteria among the diagnostic criteria of diabetes in these parts of the developing world. This discordance points out that the question of optimally predicting diabetes risk is still unsolved and needs further clarification. No study has examined diabetes incidence using repeated measures of HbA_{1c} in Iran.

The objectives of this study, therefore, were to estimate the prevalence and incidence of type 2 diabetes by current OGTT definition and the newly proposed HbA_{1c}-defined diabetes in an Iranian FDRs of patients with type 2 diabetes.

Racial disparities in HbA_{1c} values exist [13]. Comprehensive data for developing countries have not been reported. Therefore, at an ethnological level, the study contributes by characterizing the occurrence of diabetes in a specific population from central Iran.

Patients and methods

Study area

Our investigation was conducted in Isfahan, a very large area situated in central Iran, located on 1,590 m height above sea level, between latitudes 30 and 34° north of the equator and longitude 49–55° east, with a population of almost four and half million (4,559,256 in 2006 (men 2,335,399, women 2,223,857)) and a high proportion of young people. The total area is 107,029 Km². The climate is dry temperate and quite wide temperature differences between the summer and the winter with a mean daily temperature of 3.0° Celsius in January and February, 29.0° Celsius in July and August, and 16.5° Celsius in September and October. The population structure and socioeconomic status of Isfahan are similar to the rest of the country. Private physicians and hospitals, district health centers, and government and university hospitals and clinics provide the health services. Fifteen endocrinologists and 3 diabetes centers serve the study area. Residency in remote and mountain areas and economical status may affect accessibility to the endocrinological expertise.

Participants and data collection

The Isfahan Diabetes Prevention Study (IDPS) is an ongoing cohort study in central Iran to assess the efficacy

of intensive diet and exercise to prevent or delay the onset of type 2 diabetes in the FDRs of patients with type 2 diabetes. The study was performed between 2003 and 2005. A total of 3,176 (826 men and 2350 women) FDRs of a consecutive sample of patients with type 2 diabetes attending clinics at Isfahan Endocrine and Metabolism Research Center were included in the study. The participants completed laboratory tests including standard 75 g 2-h OGTT, HbA_{1c} and a questionnaire on their health status and on various potential risk factors for diabetes. Participants received follow-up tests according to a medical care standard in diabetes [14] to update information on demographic, anthropometric, and lifestyle factors and on newly diagnosed diabetes. Accordingly, if OGTT was normal at baseline, repeated testing was carried out at least at 3-year intervals. Otherwise, repeat testing was carried out annually. The IDPS baseline methods have been described in detail elsewhere [15]. The participants included siblings and children. The tenants of the Declaration of Helsinki were followed, institutional ethical committee approval was granted, and an informed consent form was signed by each participant.

Ascertainment of diabetes

Cases of diabetes were identified from baseline and follow-up OGTTs and HbA_{1c} according to American Diabetes Association criteria [2]. Pregnant women were excluded. This study used data of 923 FDRs (216 men and 707 women) who were free of diabetes at registration and had at least one subsequent review in mean (standard deviation [SD]) follow-up period of 5.0 (1.5) years and who were aged 30 years and over (Fig. 1).

Procedures

Participants reported to clinics in the morning after overnight fast. Subjects were asked to abstain from vigorous exercise in the evening before and in the morning of the investigations. Smokers were encouraged to abstain from smoking in the morning of the investigations. First on arrival at the clinic, the information given by the participants in the

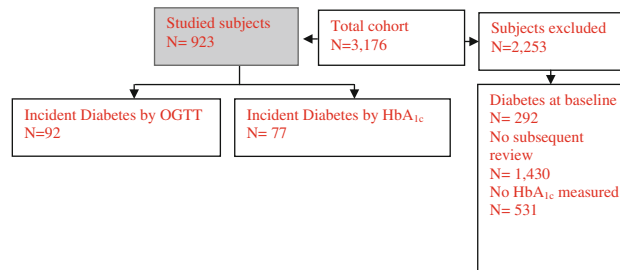


Fig. 1 Schematic diagram of the study population

questionnaire on family history was verified. Then, with the subjects in light clothes and without shoes, height, weight, waist, and hip circumference were measured using standard apparatus. Weight was measured to the nearest 0.1 kg. Height, waist, and hip circumference were measured to the nearest 0.5 cm. Waist was measured midway between the lower rib margin and the iliac crest at the end of a gentle expiration. Hip circumference was measured over the greater trochanter directly over the underwear. Resting blood pressure (BP) was measured after subjects had been seated for 10 min, using standard techniques. FPG was measured using the glucose oxidase method. All subjects underwent a standard OGTT (75 g 2-h glucose), including FPG assessment, at baseline and the follow-ups. Venous blood was sampled at fasting, 30, 60, and 120 min after oral glucose administration. Plasma samples obtained after centrifugation were analyzed the same day.

HbA_{1c} (measured by ion-exchange chromatography), total cholesterol, triglyceride, high-density lipoprotein (HDL) cholesterol, and low-density lipoprotein (LDL) cholesterol (calculated by the Friedewald equation provided total triglycerides did not exceed 400 mg/dl [16]) were also assessed at the baseline and through follow-ups. All blood sample procedures were performed in the central laboratory of the Isfahan Endocrine and Metabolism Research Center using enzyme-linked method. The same methodology was used for both the prevalence and incidence studies.

Definitions

Diabetes was defined if: (i) FPG ≥ 126 or (ii) 2-h plasma glucose of ≥ 200 mg/dl or (iii) HbA_{1c} $\geq 6.5\%$. Pre-diabetes was defined as having IFG (FPG: 100–125 mg/dl and 2-h plasma glucose < 140 mg/dl) or IGT (FPG < 126 mg/dl, but with 2-h plasma glucose concentration ≥ 140 and < 200 mg/dl) or HbA_{1c} 6.0–6.49% [17]. Whereas if the FPG was below 100 mg/dl and 2-h plasma glucose smaller than 140 mg/dl and HbA_{1c} $< 6.0\%$, it was considered a sign of normal glucose tolerance (NGT) [14, 18].

Determination of diabetes incidence

Incidence of diabetes was expressed as the number of type 2 diabetes cases per 100 person-years of follow-up. As the relevant period was considered the date of completion of the baseline examination between 2003 and 2005 until the either (i) occurrence of diabetes, (ii) the date of the last completed follow-up, (iii) death, or (iv) end of follow-up on December 31, 2009, whichever came first. For ease of interpretability, we report the incidence rates in terms of percent per year.

Statistical analysis

Statistical methods used included the Student's *t*-test, chi-squared test, analysis of variance, or Kruskal–Wallis tests for normally or non-normally distributed continuous variables, respectively, and Cox's proportional hazards model. Univariate and multivariate Cox's proportional hazards models were fitted to identify the predictors of new-onset diabetes using SPSS version 18 for Windows (SPSS Inc., Chicago, IL, USA). Variables age, BMI, waist circumference, triglyceride, LDL, HDL, total cholesterol, and BP were entered in the multivariate-adjusted analyses as continuous variables, while gender, IGT, and IFG were categorical. Adjustment for age and gender was made in separate models. Age-adjusted means were calculated and compared using general linear models. The ability of FPG, 2-h glucose values, and HbA_{1c} to predict the incidence of diabetes according to current OGTT definition or newly proposed HbA_{1c}-defined diabetes was examined by ROC curve and their respective areas under the curve, in which sensitivity was plotted as a function of 1-specificity. Areas under the ROC curves were compared by the algorithm developed by DeLong et al. [19]. All tests for statistical significance were two-tailed, confidence intervals (CI) were set at 95%, and $P < 0.05$ was considered significant.

Results

Characteristics

The baseline characteristics of the study participants by different HbA_{1c} categories are shown in Table 1. In age-adjusted comparisons of variables at baseline, age, follow-up duration, number of follow-up visits, plasma glucose at 30 and 60 min., HbA_{1c}, and diastolic BP were more likely to increase and HDL was more likely to decrease across the four subject groups. The mean (SD) age of participants was 42.9 (6.3) years and 76.6% were women.

Prevalence

Of the 3,176 subjects who received an OGTT, HbA_{1c} was measured in 2,645 (83.3%) at baseline. Of the 3,176 participants, 292 had diabetes at baseline by OGTT and the prevalence of diabetes was 9.2% (95% CI: 8.2, 10.2). Of the 2,645 participants who had HbA_{1c}, 210 had diabetes at baseline by HbA_{1c} ≥ 6.5 and the prevalence of diabetes was 7.9% (95% CI: 6.9, 9.0). Among these cases, 103 (49.0%) had diabetes according to both OGTT- and HbA_{1c}-defined diabetes, while 107 (51.0%) did not have diabetes by OGTT criteria. A total of 1,236 (38.9%) participants had pre-diabetes, including 655 (20.6%) IGT only and 581

Table 1 Age, age-adjusted, and proportion characteristics of first-degree relatives of patients with type 2 diabetes by HbA_{1c} categories in the Isfahan Diabetes Prevention Study

Characteristics	Total	HbA _{1c} level (%)			
		<5.0	5.0–5.4	5.5–5.9	6.0–6.4
Number (%)	923 (100)	446 (48.3)	240 (26.0)	150 (16.3)	87 (9.4)
Age (year)	42.9 (0.21)	42.3 (0.30)	43.0 (0.40)	43.7 (0.51)	43.8 (0.67)*
Height (cm)	159.0 (0.26)	158.8 (0.38)	159.4 (0.52)	159.0 (0.65)	159.3 (0.86)
Weight (kg)	73.1 (0.38)	72.6 (0.55)	73.7 (0.75)	72.6 (0.94)	75.0 (1.25)
Waist circumference (cm)	88.6 (0.31)	88.2 (0.44)	89.2 (0.60)	88.3 (0.76)	89.4 (1.00)
Hip circumference (cm)	107.6 (0.29)	107.6 (0.42)	107.4 (0.58)	107.6 (0.73)	108.4 (0.96)
Waist-to-hip ratio	0.82 (0.002)	0.82 (0.003)	0.83 (0.004)	0.82 (0.005)	0.83 (0.007)
Body mass index (kg/m ²)	28.9 (0.14)	28.9 (0.20)	29.0 (0.27)	28.7 (0.34)	29.6 (0.45)
Follow-up duration (year)	5.0 (0.05)	4.9 (0.07)	4.9 (0.09)	5.2 (0.12)	5.3 (0.15)*
Number of follow-up visit	2.6 (0.03)	2.6 (0.05)	2.5 (0.06)	2.7 (0.08)	2.8 (0.10)
FPS (mg/dl)	96.6 (0.42)	95.8 (0.59)	96.9 (0.80)	97.2 (1.02)	98.2 (1.33)
PG 30 min (mg/dl)	147.4 (1.09)	144.0 (1.54)	150.0 (2.11)	153.1 (2.69)	148.3 (3.59)*
PG 60 min (mg/dl)	152.4 (1.44)	147.3 (2.04)	155.7 (2.78)	157.2 (3.52)	161.0 (4.65)**
PG 120 min (mg/dl)	123.0 (1.16)	120.6 (1.66)	125.3 (2.26)	124.6 (2.86)	126.4 (3.75)
HbA _{1c} (%)	5.0 (0.02)	4.4 (0.01)	5.2 (0.02)	5.7 (0.02)	6.2 (0.03)***
Cholesterol (mg/dl)	195.9 (1.36)	194.5 (1.92)	199.8 (2.60)	195.6 (3.31)	192.7 (4.38)
LDL (mg/dl)	118.5 (1.19)	117.9 (1.67)	121.4 (2.27)	117.0 (2.92)	115.7 (3.83)
HDL (mg/dl)	44.9 (0.40)	45.7 (0.58)	45.2 (0.79)	44.5 (1.00)	41.0 (1.32)*
Triglyceride (mg/dl)	167.3 (3.55)	162.6 (5.12)	170.6 (6.96)	171.0 (8.94)	176.4 (11.76)
Systolic BP (mm Hg)	115.2 (0.56)	113.8 (0.08)	115.8 (0.10)	117.1 (0.13)	117.2 (0.18)
Diastolic BP (mm Hg)	74.6 (0.04)	73.4 (0.06)	75.1 (0.08)	76.4 (0.10)	76.5 (0.13)*
Women, no (%)	707 (76.6)	345 (77.4)	1182 (75.8)	115 (76.7)	65 (74.7)
Obesity, no (%)	329 (36.1)	157 (35.8)	83 (34.9)	56 (37.3)	33 (38.8)

Age-adjusted means were calculated using general linear models. Data are expressed as mean (SE) or number (%)

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$ comparison across all four groups

(18.3%) IFG only by OGTT criteria, and 204 (7.7%; 95% CI: 6.7, 8.8) had pre-diabetes by HbA_{1c} in the range 6.0–6.49%.

Incidence

During 4,600 (1,078 men and 3,522 women) person-years of follow-up, 92 (10.0%) (19 men and 73 women) incident cases of type 2 diabetes occurred according to current OGTT definition, while 77 individuals had diabetes by the HbA_{1c} ≥ 6.5 . The overall incidence of subsequent diabetes was 2.0% (95% CI: 1.6, 2.4) (1.8% (95% CI: 1.1, 2.7) men and 2.1% (95% CI: 1.6, 2.6) women) per year by OGTT criteria, while incidence of diabetes was 1.7% (95% CI: 1.3, 2.0) (1.6% (95% CI: 0.9, 2.5) men and 1.7% (95% CI: 1.3, 2.2) women) per year by HbA_{1c} ≥ 6.5 . Among participants with HbA_{1c} ≥ 6.5 , 31.2% had diabetes, 20.8% had IGT, 26.0% had IFG, and 22.1% had NGT by OGTT criteria.

Table 2 shows the incidence of diabetes by baseline HbA_{1c} levels. The incidence of diabetes increased across

the four subject groups, from 1.2% per year in the HbA_{1c} < 5.0 group to 3.3% per year in the HbA_{1c} = 6.0–6.4% group. Compared with participants with HbA_{1c} < 5.0 %, the risk of diabetes was 2.75 times higher in those with HbA_{1c} = 6.0–6.4% at baseline (hazard ratio (HR) 2.75; 95% CI: 1.5, 5.1) and 95% higher in those with HbA_{1c} = 5.5–5.9% (HR 1.95; 95% CI: 1.1, 3.5) in unadjusted models. Controlling for age and gender slightly reduced the HR compared with the unadjusted model. In a multivariate model, the additional adjustment for other time-dependent covariates did not appreciably alter the HR compared with the model adjusted for age and gender (Table 2). Over 80% of incident cases arose among subjects with a baseline HbA_{1c} of < 6.0 %.

The areas under the ROC curves for incidence of type 2 diabetes by HbA_{1c} ≥ 6.5 % were 0.636 (95% CI: 0.573, 0.698), 0.639 (95% CI: 0.568, 0.709), and 0.684 (95% CI: 0.619, 0.749) for the HbA_{1c}, fasting, and 2-h glucose values, respectively. The areas under the ROC curves for incidence of type 2 diabetes by OGTT-defined diabetes were 0.650

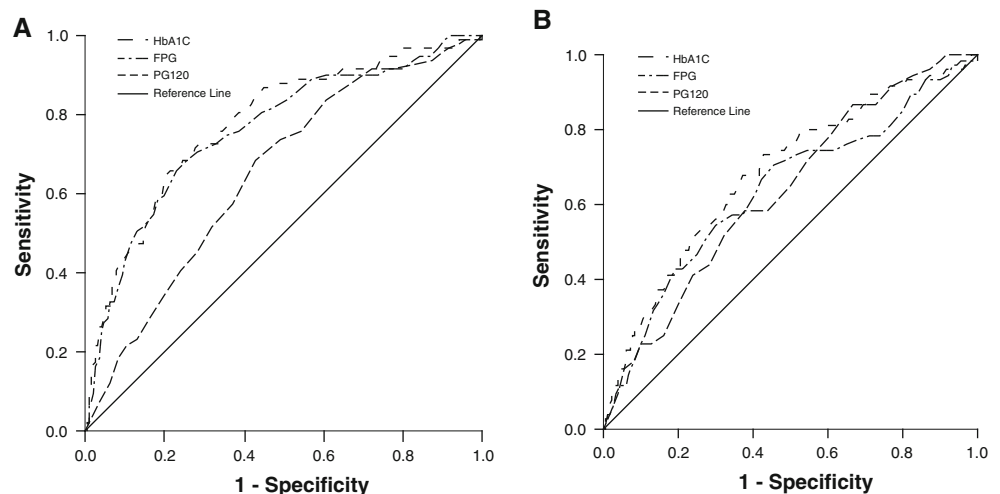
Table 2 Incidence rates and relative risks of diabetes by HbA_{1c} level and OGTT at baseline, the Isfahan Diabetes Prevention Study

	HbA _{1c} level (%) at baseline			
	<5.0	5.0–5.4	5.5–5.9	6.0–6.4
Number of cases (%)	26 (5.8)	18 (7.5)	18 (12.0)	15 (17.2)
Person-year	2,179	1,186	776	459
Incidence/100 person-year (95% CI)	1.2 (0.8, 1.7)	1.5 (0.9, 2.4)	2.3 (1.4, 3.6)	3.3 (1.8, 5.3)
Unadjusted HR (95% CI)	1.00	1.28 (0.70, 2.31)	1.95 (1.07, 3.53)	2.75 (1.46, 5.13)
Age- and gender-adjusted HR (95% CI)	1.00	1.23 (0.68, 2.25)	1.73 (0.95, 3.17)	2.47 (1.30, 4.70)
Multivariate-adjusted HR [†] (95% CI)	1.00	1.04 (0.53, 2.01)	1.73 (0.92, 3.26)	2.10 (1.00, 4.40)

CI confidence interval, HR hazard ratio

[†] Hazard ratios (with 95% CI) calculated by Cox's proportional hazards model. Adjusted for age, gender, BMI, WC, triglyceride, LDL, HDL, total cholesterol, and blood pressure

Fig. 2 Receiver operating characteristic (ROC) curves for fasting, 2-h glucose, and HbA_{1c} for prediction of type 2 diabetes by **a** OGTT- and **b** HbA_{1c}-defined diabetes in non-diabetic first-degree relatives of patients with type 2 diabetes. The estimates of the area under the ROC curves and their 95% confidence intervals are shown



Area under the curve (95% Confidence Interval)

HbA _{1c}	0.650 (0.594, 0.706)	HbA _{1c}	0.636 (0.573, 0.698)
Fasting plasma glucose	0.760 (0.705, 0.815)	Fasting plasma glucose	0.639 (0.568, 0.709)
2-hour plasma glucose	0.776 (0.724, 0.829)	2-hour plasma glucose	0.684 (0.619, 0.749)

(95% CI: 0.594, 0.706), 0.760 (95% CI: 0.705, 0.815), and 0.776 (95% CI: 0.724, 0.829) for the HbA_{1c}, fasting, and 2-h glucose values, respectively (Fig. 2). All plasma glucose concentrations were significant predictors for future risk of type 2 diabetes by either OGTT- or HbA_{1c}-defined diabetes ($P < 0.001$). The areas under the curves for 2-h PG concentration were significantly greater than those of HbA_{1c} by OGTT-defined diabetes ($P < 0.001$). 2-h PG concentration had an area slightly but not significantly larger than that of HbA_{1c} by HbA_{1c}-defined diabetes.

Discussion

This is the first follow-up study among the non-diabetic FDRs of patients with type 2 diabetes that reports the

incidence and prevalence of type 2 diabetes and relative risk for progression to diabetes according to the newly proposed HbA_{1c}-defined diabetes compared with those detected using current OGTT definition in Iran. We found an overall incidence of diabetes of 1.7% per year (77 patients) over an average follow-up of 5.0 years by HbA_{1c} ≥ 6.5 , while incidence of diabetes was 2.0% per year (92 patients) by OGTT criteria. It seems that the lower the HbA_{1c} levels at baseline, the lower the risk of progression to diabetes. Almost half of those identified by the OGTT-defined diabetes had the HbA_{1c} $\geq 6.5\%$, confirming observations from other studies [20–22]. These findings clearly demonstrate that subjects identified by HbA_{1c} $\geq 6.5\%$ are different from those classified by the OGTT criteria. Our study showed that the discriminating power of FPG and 2-h post-load plasma glucose values to distinguish between individuals at diabetes risk and

those not at risk was almost similar to that of HbA_{1c}. Even though fasting, 2-h PG, and HbA_{1c} value had approximately the same predictive power in our study, HbA_{1c} is superior in clinical practice because it is a simple test and does not need fasting state. Choosing HbA_{1c} as diabetes test avoids cost and inconveniences associated with OGTT [1].

This study shows that the prevalence and incidence rate of type 2 diabetes were lower when replacing the OGTT-defined diabetes with HbA_{1c}-defined. A recent study observing the impact of using HbA_{1c} ≥ 6.5 for detecting type 2 diabetes instead of an OGTT found four populations with a decrease in prevalence and three populations with an increase [23, 24]. The first four populations had a relatively lower mean HbA_{1c}, similar to that within this cohort, which generally favors a lower proportion of the population with HbA_{1c} $\geq 6.5\%$.

Only two studies have examined the incidence and relative risk of diabetes using repeated measure of HbA_{1c} in individuals defined by different baseline HbA_{1c} levels. Selvin et al. examined the incidence of self-reported diabetes in American men and women with different baseline HbA_{1c} values [13]. The 15-year cumulative incidence of diabetes was 6, 12, 21, and 44% in individuals with a HbA_{1c} of <5.0 , 5.0–5.4, 5.5–5.9, and 6.0–6.4%, respectively. Chamnan et al. [25] also estimated the incidence of type 2 diabetes defined by the newly proposed diagnostic criteria and/or clinically in EPIC-Norfolk Cohort categorized by different HbA_{1c} levels. The 3-year cumulative incidence of diabetes was 0.4, 0.3, 1.1, and 2.4% in individuals with a HbA_{1c} of <5.0 , 5.0–5.4, 5.5–5.9, and 6.0–6.4%, respectively. In our study, the estimated annual incidence was higher than those observed across all HbA_{1c} categories. Our study sample was addressed to individuals at increased risk of developing type 2 diabetes, because they had FDRs with the disease and it might be explained by the differences in the levels of other risk factors and in particular the different definitions of diabetes used in each study. Different studies have found that the incidence and prevalence of type 2 diabetes are greater in those persons who have a family history of the disease [26–32]. A Swedish study was found that persons with a family history of diabetes have a 2–3 times higher prevalence of both diabetes and impaired glucose metabolism than one without (27).

Similar to our findings, an international expert committee reported that people with a HbA_{1c} value of at least 6% but less than 6.5% are likely to be at highest risk for progression to diabetes [17].

Our findings are also compatible with Tsuji et al.'s; in screening test for diabetes by using the ROC curve analysis, they found that HbA_{1c} has almost the same discriminatory power as FPG [33].

A few studies [34, 35] suggest that the combined use of FPG and HbA_{1c} predicts the incidence of diabetes more

effectively than either test alone in individuals at risk of diabetes. This warranted further study.

The strengths of the present study include the prospective cohort design, the sample consisting of both men and women of a wide age range from an Iranian population, diagnosis of diabetes based on both repeat standard OGTT and HbA_{1c}, and information on potential determinants of diabetes. All participants underwent a full OGTT and HbA_{1c}, which was repeated in each follow-up visit. Selection and information bias is considered unlikely by virtue of the prospective design. Our study was addressed to individuals at increased risk of developing type 2 diabetes, because they had FDRs with the disease. The HbA_{1c} value reflects mean glycemia over the preceding 2–3 months, so people with a history of diabetes of less than 3 months might not be identified by HbA_{1c} testing. However, this is extremely unlikely given that on average a seven-year gap exists between the actual onset of diabetes and its diagnosis [36]. In addition, conditions that shorten the survival of erythrocytes, such as hemolytic anemia, will decrease the concentration of HbA_{1c}. Conversely, conditions that prolong the age of erythrocytes, such as splenectomy and aplastic anemia, will increase the concentration of HbA_{1c} independent of glycemia. Hemoglobinopathies such as hemoglobin S (sickle-cell) interfere with some assays. Thus, the use of HbA_{1c} may be inappropriate for such disorders.

However, there is a need for more studies in developing countries, including the cost-effectiveness of HbA_{1c} versus plasma glucose testing, before HbA_{1c} can be universally recommended as a diagnostic test for diabetes in developing world.

In conclusion, our study indicates that the incidence and prevalence of diabetes using newly proposed HbA_{1c} threshold in this FDRs of patients with type 2 diabetes were slightly lower than using current OGTT definition. The HbA_{1c} was almost similar to FPG and post-load glucose values for predicting new-onset diabetes. However, HbA_{1c} is superior in clinical practice because of clinical convenience and superior precision. HbA_{1c} appeared to miss a proportion of OGTT-defined diabetes cases.

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Conflict of interest None.

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