Fasting Plasma Glucose in Screening for NIDDM in the U.S. and Israel

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OBJECTIVE — To demonstrate the inadequacy of fasting plasma glucose for screening for NIDDM, even among groups at high risk for diabetes.

RESEARCH DESIGN AND METHODS — Representative samples of adults 40–69 years of age in the U.S. (n = 2,035) and Israel (n = 2,316) were selected. Fasting plasma glucose (FPG) was measured and a 2-h oral glucose tolerance test (OGTT) was administered. Subjects with undiagnosed NIDDM were identified using internationally accepted diagnostic criteria (FPG ≥7.8 mM or 2-h plasma glucose ≥11.1 mM).

RESULTS — Only 31–38% of subjects with undiagnosed NIDDM had fasting hyperglycemia (≥7.8 mM), and 36% in the U.S. and 19% in Israel had normoglycemia (<6.1 mM). Postchallenge glucose, diagnostic of diabetes, was associated with all fasting values, including values <5.0 mM. Based on sensitivity, specificity, and positive predictive value, no FPG level provided a satisfactory cutoff point to use in screening for undiagnosed NIDDM. Sensitivity at each FPG cutoff point varied little among groups classified by age, sex, race, blood pressure status, or body mass index (BMI) levels >23, but sensitivity was lower among those with BMI levels <23.

CONCLUSIONS — In the clinical setting, FPG is commonly used in screening for NIDDM. However, fasting values ≥7.8 mM are highly insensitive for detecting NIDDM. Lower FPG cutoff points that achieve acceptable sensitivity are accompanied by inadequately low specificity, require a high percentage of patients to be retested, and result in a low yield of diabetes among those screened. Clinicians and researchers who seek detection of undiagnosed NIDDM should use the OGTT, because FPG lacks adequate sensitivity and specificity for this purpose.

In 1979–1980, the National Institutes of Health National Diabetes Data Group (NDDG) and the World Health Organization (WHO) established fasting plasma glucose (FPG) ≥7.8 mM or plasma glucose ≥11.1 mM at 2 h after a 75-g oral glucose tolerance test (OGTT) as the criteria for diagnosis of non-insulin-dependent diabetes mellitus (NIDDM) in asymptomatic subjects (1,2). Although the NDDG suggested that a mid-test OGTT value also be ≥11.1 mM for diagnosis of NIDDM, essentially all individuals who meet the 2-h criterion also meet this mid-test requirement (3–5). Both the NDDG and WHO criteria require a repeat determination of fasting or postchallenge plasma glucose for a definitive diagnosis of diabetes in an asymptomatic patient; that is, the diagnosis cannot be made with a single glucose result. The recommendations of the NDDG and WHO have been accepted and endorsed by the American Diabetes Association and other national diabetes organizations representing the scientific bodies most concerned with diabetes.

In clinical practice, measurement of FPG appears to be a common method in screening for NIDDM, probably because it is simpler than OGTT and requires less time on the part of the patient and the physician. However, FPG is a very insensitive test because as many as 80% of diabetes cases discovered in population screening by OGTT have FPG values <7.8 mM (5–10). Whether sensitivity of FPG is improved in groups at high risk for NIDDM has not been addressed. Our study evaluates the effectiveness of various FPG values in screening for undiagnosed NIDDM and investigates the influence of age, sex, race, obesity, and hypertension on the sensitivity of detection of NIDDM by FPG. The data indicate that FPG is an ineffective method of screening for undiagnosed NIDDM, even in groups at high risk for diabetes.

RESEARCH DESIGN AND METHODS

— This study includes people in national population samples in Israel (5,11; n = 2,316) and the U.S. (3; n = 2,035) who are 40–69 years of age and have no medical history of diabetes. FPG was measured after a 10–16 h overnight fast, and a 2-h OGTT was administered.

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Received for publication 6 July 1993 and accepted in revised form 27 January 1994.

NDDG, National Diabetes Data Group; WHO, World Health Organization; FPG, fasting plasma glucose; OGTT, oral glucose tolerance test; NIDDM, non-insulin-dependent diabetes mellitus; BMI, body mass index.

Table 1—*Sensitivity, specificity, positive predictive value, and percentage requiring retesting in U.S. and Israel populations aged 40–69 years by different FPG cutoff points*

FPG cutoff		Sensitivity (%)		Specificity (%)		Positive predictive value (%)		Percentage requiring retesting (%)	
mM	mg/dl	U.S.	Israel	U.S.	Israel	U.S.	Israel	U.S.	Israel
≥4.44	≥80	97.5	99.4	3.7	3.9	5.7	7.2	96.3	96.3
≥4.99	≥90	92.9	97.5	31.6	18.1	7.6	8.2	69.8	83.0
≥5.55	≥100	83.1	95.0	75.9	46.7	17.2	11.8	27.4	56.2
≥6.10	≥110	65.1	80.9	93.2	83.6	36.7	27.1	10.1	20.9
≥6.66	≥120	53.6	64.8	98.2	95.4	64.6	51.7	4.7	8.8
≥7.21	≥130	42.2	49.4	99.8	99.4	91.1	87.0	2.6	4.0
≥7.77	≥140	31.1	38.3	100.0	100.0	100.0	100.0	1.8	2.7

Blood pressure, weight, and height were measured, and information on demographic characteristics and use of antihypertensive medication was obtained. WHO criteria (2) were used to classify subjects as having diabetes (FPG ≥7.8 mM or 2-h plasma glucose ≥11.1 mM). Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m^2).

Effectiveness of screening for diabetes by FPG was evaluated by calculating four measures for FPG screening cutoff points: *1*) sensitivity—the percentage with FPG levels greater than or equal to the cutoff point among those meeting diagnostic criteria for diabetes; 2) specificity—the percentage with FPG levels less than the cutoff point among those not meeting diagnostic criteria for diabetes; 3) positive predictive value—the percentage meeting diagnostic criteria for diabetes among all people with FPG greater than or equal to the cutoff point; and 4) percentage requiring retesting—the percentage with FPG levels greater than or equal to the cutoff point among all people screened (retesting is necessary because a repeat determination of fasting or postchallenge glucose is required to confirm a clinical diagnosis of diabetes [1,2]).

RESULTS— Mean FPG in subjects with newly found diabetes was 7.6 mM in the U.S and 7.9 mM in Israel, and mean 2-h postchallenge glucose was 14.6 and 15.0 mM, respectively. Thus, undiagnosed NIDDM was associated with significant hyperglycemia. FPG levels were broadly distributed among individuals with diabetes, and only 31.1% in the U.S. and 38.3% in Israel had fasting hyperglycemia (FPG ≥7.8 mM). Moreover, 34.9 and 19.2%, respectively, had FPG <6.1 mM, which is commonly considered to be normoglycemia. Even in NIDDM cases with 2-h levels that were clearly in the diabetic range (≥12.8 mM), only 40.5 and 49.0% in the two countries, respectively, had fasting hyperglycemia; normal fasting levels (<6.1 mM) were observed in 21.2 and 15.6% of subjects. A small proportion (3.4% in the U.S. and 6.1% in Israel) had fasting hyperglycemia and 2-h glucose <11.1 mM, but, for almost all of these, the 2-h value was >10.5 mM. In summary, fasting values ≥7.8 mM were almost always associated with 2-h values ≥11.1 mM, whereas 2-h values ≥11.1 mM were associated with any fasting value, even values <5.0 mM.

Table 1 presents the sensitivity, specificity, positive predictive value, and percentage requiring retesting by a confirmatory OGTT in the two populations, according to FPG cutoff points. The data demonstrate that no FPG cutoff point provides an adequate screening method. For example, at an FPG value of ≥5.55 mM for U.S. subjects, sensitivity and specificity are moderate (83.1 and 75.9%), and the percentage requiring retesting is relatively low (27.4%). However, positive predictive value is undesirably low: only 17.2% of people with FPG ≥5.55 mM met diagnostic criteria for diabetes. Thus, for every six subjects identified by such screening, only one might actually have diabetes.

Table 2 presents the sensitivity and percentage requiring retesting by confirmatory OGTT when FPG ≥5.55 mM is used as a screening criterion in various groups. Sensitivity varied little in any of the groups, with the exception of lower sensitivity among those with BMI <23. The percentage requiring retesting was lower in women than in men and in younger than in older subjects, but no major differences were noted between whites and blacks in the U.S. or among the four ethnic groups in Israel. The percentage requiring retesting was greater for obese individuals and hypertensive individuals compared with those with low BMI and normotensive individuals. Similar results were found for other FPG cutoff points (data not shown). In summary, while FPG ≥5.55 mM was relatively more effective than other FPG cutoff points (Table 1), it was inadequate for screening in the total population or in high-risk groups (Table 2).

CONCLUSIONS— As our data and those of others show, sensitivity of FPG ≥7.8 mM can range in different populations groups from 22 to 91% and is most

Table 2—*Sensitivity and percentage requiring retesting for FPG cutoff point ≥5.55 mM (100 mg/dl) in certain groups*

	U.S.		Israel	
	Sensitivity (%)	Percentage requiring retesting (%)	Sensitivity (%)	Percentage requiring retesting (%)
Sex				
Men	88.8	32.4	96.1	61.6
Women	79.6	23.1	93.1	50.7
Age (years)				
40–49	82.6	22.7	95.8	47.8
50–59	81.9	27.7	94.9	58.5
60–69	84.2	33.6	94.9	63.7
Ethnicity				
White	83.5	27.4		
Black	79.2	30.1		
Yemen			97.7	58.5
Mid-Eastern			90.7	52.8
North African			91.9	53.4
European			100.0	59.1
BMI (kg/m^2)				
<23	43.3	14.1	82.3	44.3
23–26.9	84.0	26.2	98.3	54.8
≥27	89.4	39.0	96.3	64.4
Blood pressure (mmHg)				
Normotensive	82.0	20.7	92.8	53.5
Hypertensive				
Untreated	82.7	36.0	100.0	59.7
On AHM	84.5	39.9	95.5	66.6
Total	83.1	27.4	95.0	56.2

Hypertension defined by systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg or use of antihypertensive medications (AHM), including diuretics.

commonly <35%. If an FPG cutoff point low enough to ensure minimally adequate sensitivity is used (e.g., ≥5.55 mM, Table 1), specificity and positive predictive value are too low. Thus, if FPG is used for screening, the alternatives are high sensitivity at the expense of low specificity or vice versa. Other methods of screening for undiagnosed NIDDM have been investigated and also found to be inadequate. Glycosylated hemoglobin and glycosylated total serum proteins have the same advantages as FPG, requiring only one blood sample and minimal patient cooperation, and they are not affected by time of day or recent food intake. However, they are unsatisfactory for screening because their distributions overlap extensively between diabetic and nondiabetic groups (5,12–15). Casual and random glucose are not acceptable screening methods because these cannot be standardized with regard to risk of having diabetes or developing its complications because of the considerable fluctuations of plasma glucose levels according to the time interval from the preceding meal and the unstandardized content of the meal. Thus, screening by any of the above methods does not provide adequate sensitivity and specificity. Only the OGTT provides sensitivity and specificity desirable in screening for undiagnosed NIDDM, even in high-risk groups.

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