Evaluation of Fasting Plasma Glucose as Screening Test for NIDDM in Older Adults

Rancho Bernardo Study

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Objective: To examine the efficiency of fasting plasma glucose (FPG) as a screening test for non-insulin-dependent diabetes mellitus (NIDDM). Research and Methods Design: A population-based evaluation was made of FPG as screening test for NIDDM in an upper middle-class white community of Rancho Bernardo, California. NIDDM was defined by 2-h postchallenge plasma glucose (PCPG) level ≥11.1 mM, the cutoff point recommended by the World Health Organization. Participants comprised a population-based sample of 1851 men and women 50–79 yr of age that represented 80% of surviving participants surveyed between 1972 and 1974 for the Lipid Research Clinic Prevalence Study. Those with insulin-dependent diabetes were excluded. Results: Analyses were stratified by age after logistic regression indicated that FPG and age (but not gender) were significantly related to probability of disease. As FPG cutoff points increased, sensitivity and percentage of the population to be recalled for confirmation decreased, whereas specificity and positive predictive value increased. Negative predictive value was consistently in the 90% range. Specificity did not change with age. In contrast, at virtually every FPG cutoff point, sensitivity decreased with increasing age. For example, at FPG ≥6.7 mM, sensitivity was 65.6% for those 50–64 yr of age and 40.0% for those 65–79 yr of age. At FPG ≥7.2 mM, these sensitivites were 46.9 and 28.5%, respectively. Positive predictive value increased with increasing age, reflecting the increasing prevalence of NIDDM with age. Conclusions: Poorer sensitivity with increasing age reflects the fact that the numerator of the sensitivity equation is not affected by age (mean FPG did not vary significantly between age-groups), whereas the denominator increases with age (mean PCPG increased from 6.6 mM for subjects 50–64 yr of age to 8.2 mM for subjects 65–79 yr of age). Nevertheless, because the clinical significance of increasing PCPG with age in older adults is unknown, age-specific screening criteria probably are not warranted. *Diabetes Care* 14:989–93, 1991

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The prevalence of non-insulin-dependent diabetes mellitus (NIDDM) is increasing worldwide, especially in recently affluent or economically advanced countries. This is believed to reflect increasing obesity and decreasing physical activity in industrialized societies (1). Twenty years ago, there was considerable interest in mass screening for diabetes to prevent debilitating or fatal complications. Current enthusiasm for early screening and diagnosis is tempered by questions about the benefit of early diagnosis and treatment and the risks of labeling, where the diagnosis of diabetes may carry economic, social, physical, and psychological consequences (2–4). The issue is still under debate (5,6).

There is no accepted screening test for diabetes short of an oral glucose tolerance test (OGTT). This test is expensive and time consuming compared with other blood tests that require venipuncture and no glucose load. A screening protocol has been proposed in which only those with fasting plasma glucose (FPG) ≥6.4 mM receive a positive OGTT (1,7). In this study, we examined different levels of FPG as a screening test for NIDDM in older adults to determine whether there is a

level that efficiently defines those for whom being recalled for an OGTT would be most useful.

RESEARCH DESIGN AND METHODS

Between 1972 and 1974, 82% of all adult residents of an upper middle-class white community in Rancho Bernardo, California, participated in a survey of heart disease risk factors as part of the Lipid Research Clinic Prevalence Study (8). Between 1984 and 1987, 80% of surviving participants ≥40 yr of age at the baseline visit were studied for diabetes and other chronic diseases. A standard 75-g OGTT was performed in the morning after a 12-h fast. Blood was drawn by venipuncture before and 2 h after the glucose load. Plasma glucose levels were measured in a diabetes research laboratory with a glucose oxidase method. Participants were also interviewed by standard questionnaire about history of diabetes and use of diabetic medications (9).

The participants were 801 men and 1050 women 50–79 yr of age at the time of the 1984 to 1987 screening, who had both FPG and postchallenge plasma glucose (PCPG) results, and could be categorized accurately for diabetes status (75%). There were 63 participants with NIDDM based on prior diagnosis and diabetes medication use. Seven individuals with insulin-dependent diabetes mellitus, defined by use of insulin in the past 2 wk and a C-peptide level <0.60 pM (n = 5) or diagnosis of diabetes before 40 yr of age (n = 2), were excluded. Because the OGTT is necessary to detect the two-thirds of the Rancho Bernardo population with diabetes who by current criteria do not have fasting hyperglycemia (10), for this study, NIDDM was defined by 2-h PCPG levels ≥11.1 mM, the cutoff point recommended by the World Health Organization (WHO; 11).

A logistic regression model was fitted with FPG, sex, age, and all interaction terms to determine the individual and joint effects of these variables on the odds of having NIDDM. Age ($P < 0.001$) and FPG ($P < 0.001$) were significantly associated with NIDDM; gender was not. No interactions were significant. Therefore, subsequent analyses were stratified by age, not gender.

FPG cutoff points from 4.4 to 7.8 mM by 0.6-mM increments were studied as screening tests for NIDDM. Sensitivity, specificity, positive (PPV) and negative (NPV) predictive values, and percentage of population to be recalled for an OGTT were calculated at each FPG cutoff point for different age-groups. Differences between age-groups at a particular FPG cutoff point were tested by χ^2 test.

Sensitivity is the proportion of those who have NIDDM who test positive at a given FPG level, i.e., true positives. Specificity is the proportion of those who do not have NIDDM who test negative at a given FPG level, i.e., true negatives. PPV is the ratio of true positives to all who have a positive test. NPV is the ratio of true negatives to all who have a negative test. Unlike sensitivity and specificity, predictive values depend on the prevalence of the disease in the population studied, such that a higher prevalence results in a higher PPV (and a lower NPV). Percentage to be recalled for OGTT is the percentage with FPG at or above the designated level among all subjects.

Analyses were run both with and without previously known diabetic subjects. The results were very similar, with the sensitivities and PPVs being slightly lower when the known NIDDM cases were excluded. The analyses reported here include known NIDDM cases, and results were compared with a similar population tested by Haffner et al. (12).

RESULTS

Of the 1851 participants, 197 (10.6%) had NIDDM by the 2-h PCPG criteria. The prevalence of NIDDM increased with increasing age in both sexes (Table 1). Mean FPG remained remarkably stable with increasing age, whereas mean PCPG showed a stepwise increase (Fig. 1).

Figure 2 shows the sensitivities at each 0.6-mM FPG cutoff point from 4.4 to 7.8 mM in younger versus older age-groups. Sensitivities declined with increasing FPG and were consistently higher for those 50–64 yr of age compared with those 65–79 yr of age. χ^2 tests indicated significant differences ($P < 0.05$) in sensitivity between the two age-groups at FPG cutoff points 5.5–7.2 mM.

Specificity increased from 2% at the 4.4-mM cutoff point to 99% at 7.8 mM and did not differ significantly by age (Fig. 3). FPG cutoff points ≥6.1 mM had a ≥90% ability to correctly identify individuals without diabetes.

Figures 4 and 5 show PPV and NPV by FPG cutoff points and age-group. As expected, PPV increased consistently with increasing FPG, and the older age-group consistently had higher PPVs. PPVs in the two age-groups were significantly different ($P < 0.04$) at all FPG cutoff points except 5 and 7.2 mM. NPV was essentially the same at all levels of FPG, ranging from 89 to 100% and varying only slightly by age.

Table 2 summarizes the screening results with FPG cutoff points of 6.1 and 7.8 mM. At 6.1 mM, the sensitivity and specificity were ~88% for the younger age-

TABLE 1
Prevalence (n) of non-insulin-dependent diabetes mellitus (NIDDM) in men and women by age in Rancho Bernardo, California, 1984–1987

			NIDDM	
Age (yr)	Men	Women	Men	Women
50–59	163	206	11 (6.7)	5 (2.4)
60–69	249	321	24 (9.6)	23 (7.2)
70–79	389	523	69 (17.7)	65 (12.4)

Percentages in parentheses.

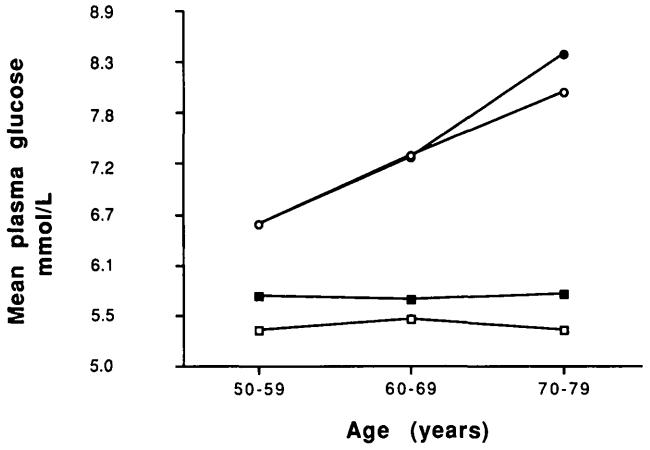

FIG. 1. Mean fasting plasma glucose (FPG) and post-challenge plasma glucose (PCPG) by age and sex in Rancho Bernardo, California, 1984 to 1987. ●, PCPG men; ○, PCPG women; ■, FPG men; □, FPG women.

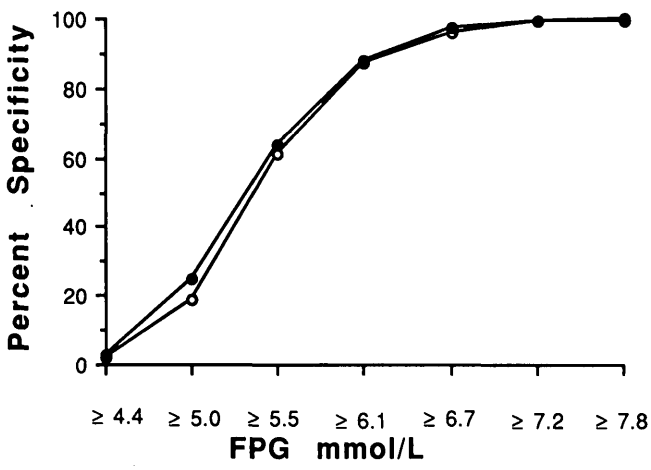

FIG. 3. Specificity by fasting plasma glucose (FPG) levels and age in Rancho Bernardo, California, 1984–1987. ○, 50–64 yr of age; ●, 65–79 yr of age.

group, but the older age-group had a significantly lower sensitivity of 60% (P = 0.003). The PPV was low for both groups but significantly higher for the older age-group (P = 0.002). At 7.8 mM, specificity for both groups was ~99%, but sensitivity dropped to 31 and 21% for the younger and older age-groups, respectively. PPV increased but remained significantly higher for the older age-group (P = 0.02).

CONCLUSIONS

The main purpose of a diabetes screening program is to identify asymptomatic individuals with NIDDM so that early intervention can prevent or reduce the consequences of disease. Controversy surrounds the evidence for the benefit of early intervention (13). Morsiani (1) states that according to a WHO report, the "early diagnosis and effective control of hyperglycemia in asymptomatic and oligosymptomatic diabetics can reduce the morbidity of the disease." However, Singer et al. (3) reviewed the literature and concluded that screening was not useful in reducing complications. Genuth et al.'s (2) 5-yr prospective study found meaningful therapeutic benefits in <50% of their positive screenees, but some did benefit. The consensus is that diabetes screening programs, if any, should target high-risk populations. This agrees with an American Diabetes Association policy statement that recommends screening for specific groups at high risk, including those with obesity; family history of diabetes; a history of impaired glucose tolerance, gestational diabetes mellitus, hypertension, or hyperlipidemia; or certain ethnic backgrounds (14).

Current WHO diagnostic criteria require two positive OGTTs. However, the use of any OGTT for screening

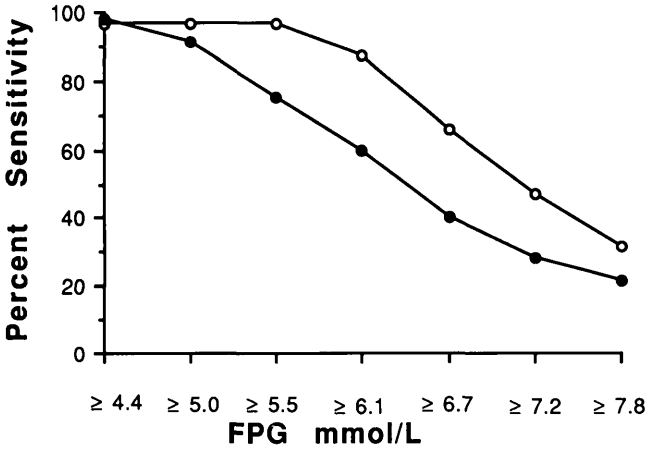

FIG. 2. Sensitivity by fasting plasma glucose (FPG) levels and age in Rancho Bernardo, California, 1984–1987. ○, 50–64 yr of age; ●, 65–79 yr of age.

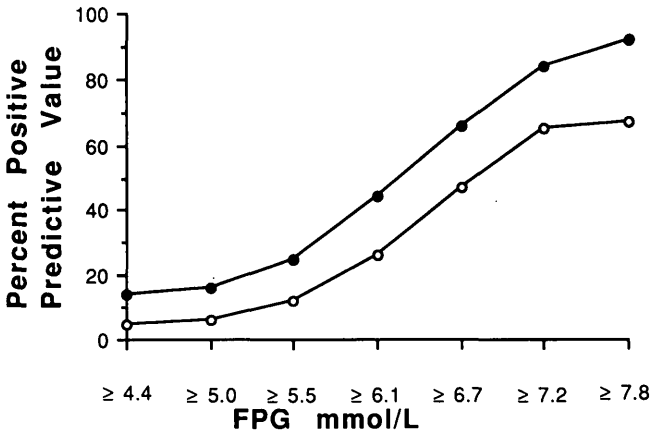

FIG. 4. Positive predictive value by fasting plasma glucose (FPG) levels and age in Rancho Bernardo, California, 1984–1987. ○, 50–64 yr of age; ●, 65–79 yr of age.

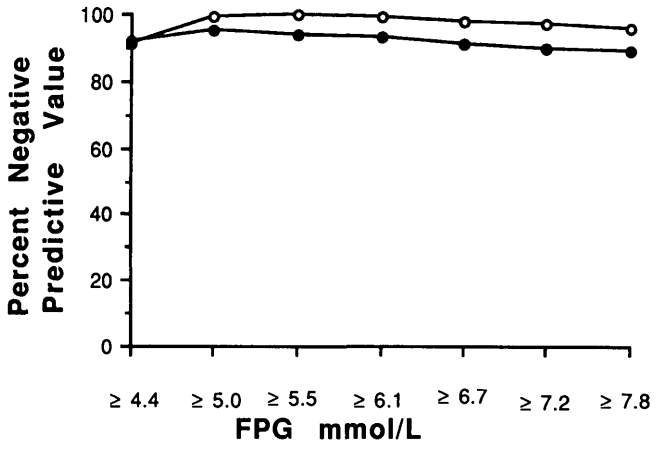

FIG. 5. Negative predictive value by fasting plasma glucose (FPG) levels and age in Rancho Bernardo, California, 1984–1987. ○, 50–64, yr of age; ●, 65–79 yr of age.

TABLE 3
Comparison of percentage recalled for confirmation testing of non-insulin-dependent diabetes mellitus (NIDDM) in Rancho Bernardo, California, and San Antonio, Texas, cohorts

Fasting plasma glucose (mM)	Rancho Bernardo*	San Antonio†
≥4.4	97.2	
≥5.0	87.5	
≥5.5	41.4	20.8
≥6.1	17.9	8.5
≥6.7	7.8	4.5
≥7.2	4.3	2.9
≥7.8	2.9	2.0

*Whites, 50–79 yr of age, 10.6% with NIDDM.
†Anglo-Americans, 25–64 yr of age, 5.5% with NIDDM (data from ref. 12).

has distinct disadvantages: patient preparation, a long visit to the screening site, administration of a glucose load with possible side effects, and at least two venipunctures or the use of an intravenous catheter. Patient resistance could be a problem if they have had a previous OGTT.

In contrast, FPG has several points that make it attractive for preliminary screening. The procedure is faster and less expensive, only requiring an overnight fast, one venipuncture, and no waiting (12). The intrapersonal variation in repeated tests is less than that for PCPG (15). (A possible concern is that the FPG in this study was part of the OGTT done on the same day, rather than days or weeks later as would occur in a clinical setting. Because FPG varies little over time, these results should parallel those obtained in a clinical setting.)

The use of FPG to effectively screen for NIDDM reduces the number of patients who must undergo an OGTT. However, the percentage of patients recalled for an OGTT will vary depending on the prevalence of hyperglycemia and diabetes in the population. Table 3 compares the percentage of the population who would be recalled for OGTT in whites from Rancho Bernardo and in Anglo-Americans from the San Antonio Heart Study (12). The percentage recalled was consistently higher for the Rancho Bernardo group, especially at the 5.5- and 6.1-mM FPG cutoff points, where the rates were twice as high as those in San Antonio. This reflects the different age ranges and non–age-adjusted prevalence of NIDDM in these cohorts (50–79 yr of age and 10.6% NIDDM in Rancho Bernardo vs. 25–64 yr of age and 5.5% NIDDM in San Antonio). The definition of disease in San Antonio differed slightly from that used here, by including cases with FPG ≥7.8 mM when the PCPG was <11.1 mM. However, with the same criteria, the number of cases in Rancho Bernardo would have increased only by eight.

Picking an optimum FPG cutoff point to screen for NIDDM is difficult, given the striking age variation in PCPG but not FPG and the need to balance true and false positives and negatives. Several papers report a mean increase in FPG of 0.06 mM/decade, whereas the mean increase in 2-h PCPG was 0.28 mM/decade (range 0.056–0.61 mM) (1,16–19). Age-related differences are very similar in prospective and cross-sectional studies (16). Similar trends with stable FPG and increasing PCPG by decade of age were found in the Rancho Bernardo population (Fig. 1). Mean PCPG for the combined sexes increased 0.7 mM from the 6th to 7th decade and 0.9 mM from the 7th to 8th decade. Consequently, in an older population, sensitivity decreases with increasing FPG cutoff points, because the denominator of the sensitivity equation increases (reflecting increasing PCPG), but there is no balancing increase in the numerator (reflecting level FPG). Similarly, specificity increases because the denominator decreases without a balancing decrease in the numerator. In the elderly, PPV increases because of increased prevalence. In Rancho Bernardo, NPV varied little with FPG level.

TABLE 2
Screening test results for various fasting plasma glucose (FPG) cutoff points by age in Rancho Bernardo, California, 1984 to 1987

	Age (yr)			
	FPG ≥6.1 mM		FPG ≥7.8 mM	
Screening test (%)	50–64	65–79	50–64	65–79
Sensitivity	88	60*	31	21
Specificity	87	80	99	100
Positive predictive value	26	44*	67	92†
Negative predictive value	99	93	96	89
Percent recalled	17	18	2.4	3.1

*$P < 0.01$, †$P < 0.05$, vs. younger age-group.

Both sensitivity and PPV also varied significantly between younger and older age-groups, reflecting the increase in PCPG with age.

The important question remains whether the increase in mean PCPG with age is a phenomenon of normal aging or indicative of increased disease (16,17). Use of a diabetes screening test that changes little with age, such as FPG, could either reduce bias when testing older populations or miss more disease in the elderly. In the absence of better data on the clinical significance of postchallenge hyperglycemia in the elderly, it is difficult to say whether cutoff points should vary by age.

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