IJMS
Vol 29, No 1, March 2004

Original Article

Evaluation of Different Risk Factors for Early Diagnosis of Diabetes Mellitus

S. Habibi Moeini, P. Mirmiran, Y. Mehrabi, F. Azizi

Abstract

Background: The efficacy of various screening variables in detection of diabetes mellitus (DM) is unclear.

Objective: To determine the efficacy of various diagnostic tests for type 2 DM.

Methods: 1021 inhabitants of Hakimieh district of Tehran aged between 30 and 75 years were studied. Known cases of diabetes and those with factors influencing glucose tolerance test were excluded. Age, sex, family history of DM, history of gestational diabetes, body mass index (BMI), waist hip ratio, blood pressure, urine glucose 2 hours after breakfast, fasting plasma glucose (FPG) and serum glucose 2 hours after consumption of 75 gm glucose (2hPG) were determined. Sensitivity, specificity and predictive values of each of these variables in comparison to WHO criteria were assessed.

Results: According to WHO criteria, 5.9% of the population had undiagnosed diabetes. This rate declined to 3.8 % when employing the latest American Diabetes Association (ADA) diagnostic criteria (FPG≥126 mg/dl). 88% of these newly diagnosed diabetics were diagnosed by means of 2hPG of whom 15% were classified within the normal group by ADA criteria. The 2hPG test showed higher reproducibility than the FPG test (84% *vs.* 67%). Truncal obesity had the maximum sensitivity (67%) and glycosuria had the highest specificity (99%). Therefore, none of these indices could be considered as a reliable screening method. Regarding 87% sensitivity and 54% specificity, a single method can be used as a proper screening test for men under 50 years of age. In women of similar age, two positive risk factors might be recruited as a useful screening method. However, the sensitivity and specificity approximated 82% and 59%, respectively.

Conclusion: 2hPG is the most reliable test for diagnosis of DM. Screening via risk factors is not useful in people older than 50 years. Individuals aged <50 years, men with at least one positive risk factor and women with a minimum of two positive risk factors, are appropriate candidates for final diagnosis by glucose tolerance test.

Iran J Med Sci 2004; 29(1):21-25.

Keywords • Diabetes Mellitus • Diagnosis • Screening

Endocrine and Metabolism Research Center, Shaheed Beheshti University of Medical Sciences, Tehran, Iran.

Correspondence: F. Azizi, MD, P.O. Box 19395-4763, Tehran, Iran
Tel: +98-21-2402463
E-mail: azizi@erc.ac.ir

Introduction

Numerous complications of diabetes mellitus (DM) account for the major causes of disability, organic defects and mortality.[1-6] Epidemiological studies have shown a prevalence of 5% to 8% DM in people over 30 years of age in some cities and in rural areas of Tehran province.[7-9] The prevalence of impaired glucose tolerance (IGT) is roughly the same as that of DM.[9,10] Thus, 16% to 20% of the populations over 30 years are expected to show abnormal glucose tolerance tests. In Iran, a national program for controlling DM and screening of high risk groups by health-care personnel has been implemented.[10]

Several methods are used for diagnosis of DM of which the most important is the oral glucose tolerance test (OGTT), that is, the measurement of blood glucose 2 hours after consumption of 75 gr of glucose given orally.[11] However, conducting OGTT in large populations is costly and cumbersome. In addition, OGTT is not available in all Iranian health networks. Hence, it would be beneficial to compare various screening methods and choose the most practical and available tests in health-care centers, to ensure the success of nation-wide control program. The aim of the present study was to evaluate, as a cost beneficial procedure, the value of various diagnostic tests for diagnosis of DM in the population of a district in Tehran, in order to detect variable(s) for practical screening of DM.

Patients and methods

Individuals between 30 and 75 years of age were selected from Hakimieh district in Northeast Tehran, by cluster sampling. Assuming 5% prevalence of unknown diabetes, 90% confidence level and 1% maximum error, 1021 cases were selected from 25000 inhabitants of the district. The exclusion criteriae were known cases of DM, patients who had been bedridden for any reasons, those afflicted by systemic diseases or infections and individuals receiving glucocorticoids or oral contraceptives.

On the first day, urine specimens were collected for glucose measurement 2 hrs after regular breakfast. Personal medical and family histories of DM were collected by questionnaires. Positive history of gestational diabetes mellitus (GDM) was considered if a woman gave a history of GDM and history of having a child with a birth weight >4000 g. Weight and height were measured. Supine arterial blood pressure, waist and hip circumferences were determined. Truncal obesity was defined according to weight-height ratio (WHR) gold standard and was 0.8 in women and 0.95 in men.

On the next day, OGTT was performed. At least 3 days prior to GTT, each individual had a diet containing a minimum of 150 g of carbohydrates and a regular physical activity. Before testing, patients fasted overnight for 10–16 hrs and received a glucose solution (1.75 grams anhydrous glucose/kg of body weight). On the day of the experiment, a venous blood sample was taken to obtain fasting blood glucose level (FBG). Then the patient was given an oral glucose solution containing 75 g of glucose in 250–300 ml of water within five min and a second blood sample was collected after 2 hrs for determination of 2h plasma glucose level (2hPG).

The standard tests were repeated on 37 of 60 known diabetic patients to confirm the reproducibility of the tests. A second GTT was performed 8 weeks later. Blood glucose levels were measured by glucose-oxidase enzymatic method. According to the WHO criteria, individuals with 2hPG levels $\geq$200 mg are considered diabetics.[12] In addition, according to the American Diabetic Association (ADA) criteria, patients with FPG levels $\geq$126 mg/dl were evaluated as diabetic.[13] In comparison with WHO criteria (2hPG$\geq$200), sensitivity, specificity, positive and negative predictive values (PPV and NPV) were calculated for each of the factors evaluated. The following preconditions were applied to the screening method in order to achieve the desired objective. 1) High sensitivity as compared to WHO criteria (>80%). 2) Low prevalence rates (<50%) of the variables or high specificity (>50%) in the population under study. The comparison group included 60 sex- and age-matched individuals selected from 961 normal subjects. Student t test was used to compare variables between two groups.

Statistical analysis

Data are presented as mean±SD. Unpaired Student t test was used to compare variables between the two groups. A p value <0.05 was considered statistically significant.

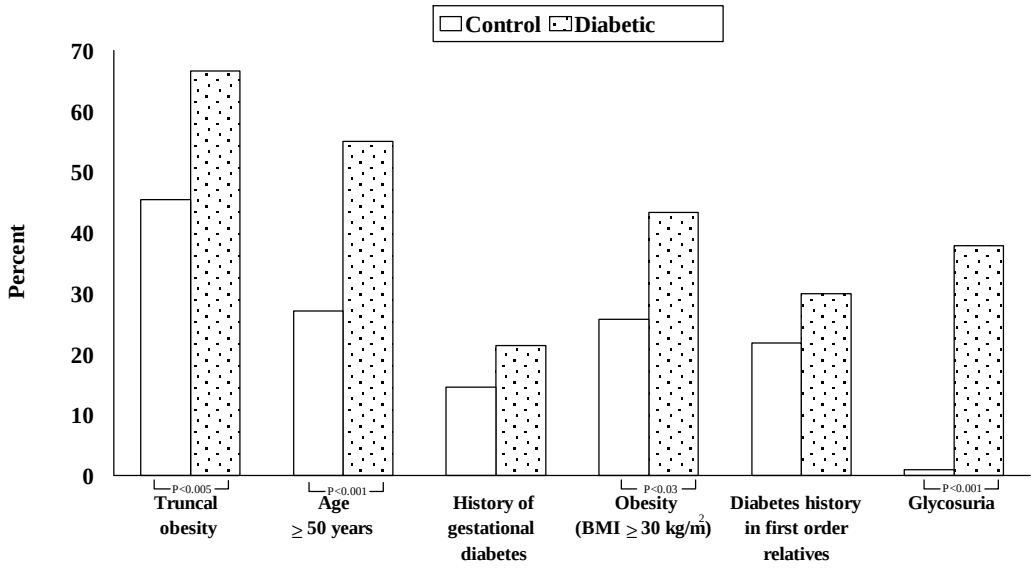

Fig 1: Relative prevalence rates of major risk factors in normal and diabetic subjects

Results

Prevalence:

Out of 1021 cases studied, 60 new diabetic patients (5.9%) were found. Fifty-two (87%) and 39 patients (65%) were diagnosed by means of 2hPG and FPG, respectively. The FPG in nine patients were between 100–110 mg/dl and in four cases it was <100 mg/dl.

Correlation coefficient (*r*) between FPG and 2hPG was 0.762 for all subjects (p<0.001). The following linear relation between FPG and 2hPG was discovered in the 60 newly diagnosed diabetic patients:

FPG = –46.83 + 0.73 2hPG, (R^2=0.68).

Reproducibility of the test was 84% (31 out of 37) with 2hPG and 67% (25 out of 37) with FPG.

Comparative study of diabetics and normal subjects:

The female to male ratio was 1.33. Among 1021 cases studied, 53.7%, 37.0% and 9.3% aged 30–44, 45–59 and >59 years, respectively. The corresponding ratios for the diabetic group were 23.3%, 46.75% and 30.0%, respectively. Overall, 28.7% of normal and 55% of diabetic subjects aged >49 years. Values of the quantitative variables for 60 normal and 60 DM cases are shown in Table 1. Significant differences between the two groups were observed for BMI (p<0.02), FPG (p<0.001) and 2hPG (p<0.001).

Relative prevalence rates of risk factors for cardiovascular disease in the two groups are demonstrated in Fig 1. Significant statistical differences were found for factors such as truncal obesity (p<0.005), obesity (p<0.03), ages of ≥50 years (p<0.001) and detection of glucose in urine (p<0.001). A significant difference (p<0.001) was also found between the two groups for detection of glucose in urine.

Values of different factors for screening:

Among all the indices studied, 6 indices including truncal obesity, age ≥50 years, obesity, history of gestational diabetes (only in

Table 1: BMI, WHR, blood pressure, FPG and 2hPG in normal and diabetic subjects

Variables	Normal subjects (n=60)		Diabetics (n=60)	
	Mean±SD	95% CI*	Mean±SD	95% CI
BMI (Kg/m^2)	27.3±3.8	26.3-28.3	29.2±4.0‡	28.1-30.2
WHR	0.89±0.07	0.87-0.91	0.90±0.07	0.88-0.92
Systolic BP (mm Hg)	133±20	128-138	132±17	127-136
Diastolic BP (mm Hg)	81.2±9.9	78.6-83.7	80.3±8.7	78.1-82.6
FPG (mg/dl)	89.2±9.4	86.7-91.6	148±48.1†	135-160
2hPG (mg/dl)	113±28.7	105-120	250±69†	232-268

* CI: Confidence interval for mean

† p<0.001, ‡ p<0.02, compared to normal subjects

Table 2: Performance characteristics of variables obtained by the standard diagnostic method for diabetes, recommended by WHO

Variables	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Truncal obesity	66.7	54.5	8.4	91.6
Age ≥ 50 years	55.0	72.9	11.3	96.3
BMI ≥ 30 Kg/m^2	43.3	74.2	9.6	95.4
Glycosuria	38.0	99.0	68.8	96.3
History of gestational diabetes	21.4	85.4	7.1	95.5
History of DM in relatives	30.0	78.0	7.9	94.7

women), diabetes history in first order relatives and glycosuria showed the highest values for the screening tests. In Table 2, sensitivity, specificity and PPV and NPV of the six aforementioned indices are compared with the standard diagnostic method recommended by WHO. The highest and lowest rates of sensitivity belonged to truncal obesity and history of GDM respectively.

Men and women were divided into four groups according to the age and sex (*i.e.*, women <50 years, women aged ≥50 years, men <50 years and men aged ≥50 years). Table 3 shows the sensitivity, specificity, PPV and NPV of the test, when at least one and two variables were positive for the four groups. When glycosuria was excluded, no significant changes in performance characteristics occurred.

In Table 4, the standard diagnostic method of diabetes is compared in terms of sensitivity, specificity, PPV and NPV when age 50 years and above was considered as a risk factor for DM. The diagnostic methods used for this Table were based upon at least one or two positive clinical indices, excluding glycosuria index. When BMI of ≥27, instead of ≥30 kg/m^2 and age of ≥45 instead of ≥50 years were employed, the sensitivity and specificity of variables could not be used for diagnosis.

Discussion

This study demonstrated that OGTT rather than fasting blood glucose is the most reliable method for the diagnosis of the undetectable diabetes mellitus. The major finding of the present investigation is that diagnostic risk factors for detection of DM are not useful for patients aged ≥50 years. People aged <50 years, men with at least one risk factor and women with at least two risk factors, were the most appropriate candidates for performing OGTT.

The prevalence rate of 5.9% for newly diagnosed diabetes in subjects >30 years is similar to the results obtained from other populations.[14] In the present study, 2hPG test had a higher sensitivity (87%) as compared to the FPG (65%) for the diagnosis of DM. About one-third of diabetic patients could not be diagnosed with FPG as recommended by ADA criteria. The expert committee proposed that individuals with an FPG <110 mg/dl is considered as normal and stated that FPG had a higher reproducibility than 2hPG.[13] However, 15% of diabetic patients enrolled in this study had FPG <100 mg/dl and their 2hPG showed a much higher reproducibility than FPG. It is possible that an inappropriate time interval between the last meal and collection of samples for measurement of FPG, could result in less reproducibility, while inappropriate interval had less negative influence on the 2hPG test.

Comparison of the normal and diabetic groups revealed that 27% of the normal individuals aged ≥50 years, and 55% of the diabetic patients were classified in this age group. This is consistent with the findings of other studies,[14] that the increment of age was a risk factor for type 2 DM.

The evaluation of data for different variables revealed that truncal obesity had the highest and history of gestational diabetes had the lowest sensitivity, respectively. In addition, glycosuria showed the highest specificity. Therefore, none of these variables *per se* could be used as a reliable diagnostic tool.

The Expert Committee recommended that all populations' aged ≥45 years should take the FPG test, while those <45 years should be screened for other risk factors.[13] Our survey also revealed the importance of detecting risk

Table 3: Performance characteristics of the positive results of at least one variable and two variables obtained by the standard diagnostic method for diabetes, recommended by WHO

Sex / Age (years)	Sensitivity (%)		Specificity (%)		PPV (%)		NPV (%)	
	1*	2	1	2	1	2	1	2
Women < 50	91.7	75.0	26.0	63.0	3.1	5.0	99.2	99.0
Women ≥ 50	94.1	70.6	7.8	47.8	16.2	20.3	87.5	89.6
Men < 50	86.7	60.0	53.6	87.5	10.7	23.7	98.4	97.1
Men ≥ 50	75.0	50.0	40.7	84.3	10.8	23.5	94.4	94.6

* 1: At least one variable; 2: At least two variables

Table 4: Performance characteristics of the positive results with at least one or two variables obtained by the standard diagnostic method for diabetes, recommended by WHO

No. of variables & sex	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Women with at least one factor	96.6	21.8	6.1	99.2
Women with two factors	82.7	54.5	8.8	98.4
Men with at least one factor	90.3	31.3	9.2	97.7
Men with two factors	54.8	68.2	11.7	95.1

factors in individuals aged <50 years (one risk factor for men, two risk factors for women). However, based on the present findings, this method could not be recommended for those aged ≥50 years.

In conclusion, with respect to the results of this survey, the following methods can be recommended for national programs: The most reliable method for the detection of undiagnosed cases of DM is the measurement of plasma glucose levels 2 hours after glucose intake (2hPG). In men <50 years of age one positive risk factor and in women <50 years, two positive risk factors are the most reliable and effective methods to use for the screening of early diagnosis of type 2 DM. However, the employment of risk factors as a screening method for individuals aged ≥50 years is not appropriate and application of 2hPG after OGTT is therefore recommended for this age group.

References

1 King H, Aubert RE, Herman WH: Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. *Diabetes Care 1998;***21:** 1414-1431.

2 Nicolussi A., Carinci F, Ciampi A: Stratifiying patients at risk of diabetic complications.*Diabetes Care 1998;***21:** 1439-1444.

3 Bild DE, Selby JV, Sinnock P, et al: Lower-extremity amputation in people with diabetes: epidemiology and prevention. *Diabetes Care 1989;***12:**24-31

4 Garcia M., McNamara J., Goijon T, et al: Morbidity and mortality in diabetics in the Framingham population: sixteen year follow-up study. *Diabetes 1994;***23:**105-11.

5 Klein R., Klein BED., Moss SE: Relation of glycemic control to diabetic microvascular complications in diabetes mellitus. *Ann Intern Med 1996;***124:**90-96.

6 Moeini S, Sheikholeslami FH. Navai L., Azizi F: Prevalence of micro-and macrovascular complication of diabetes. Proceeding of the 10th AOCE, Beijing, China, Oct 30th-Nov 3rd, 1994.

7 Larijani B, Bastanhagh M, Pajouhi M, et al. Prevalence of NIDDM in Tehran. Proceedings of the Third International congress on Endocrine Disorders, Tehran, September 4-8, 1995.

8 Amini M, Afshin-Nia F, Bashardous N, et al: Prevalence and risk factors of diabetes mellitus in the Isfahan city population (aged 40 or over) in 1993. Diabetes Res Clin Practive 1997;**38:**185- 190,

9 Azizi F: Diabetes Mellitus in the Islamic Republic of Iran. *IDF Bulletin 1996;***41:**38-9.

10 Azizi F: Diabetes Mellitus in the Islamic Republic of Iran. Assignment Report, WHO-EMRO, Dec. 1 & 7-23, 1996.

11 Engelgau MM, Thompson TJ, Aubert RE: Herman WH. Screening for NIDDM in nonpregnant adults: A review of Principles, screening tests, and recommendations. *Diabetes care 1995;***18:**1606-18.

12 Definition, diagnosis and classification of diabetes mellitus and its complications. Report of a WHO consulation, WHO, Geneva, 1999.

13 American Diabetes Association: Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care 1997;***20:** 1183-1197.

14 Harris MI, Flegal JM, Cowie CC, et al: Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults. *Diabetes Care 1998;***21:** 518-524.