Original article

IN WHICH PATIENTS WILL PERFORMING AN ORAL GLUCOSE TOLERANCE TEST YIELD THE HIGHEST RATE OF POSITIVE RESULTS ?

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Key words: Impaired glucose tolerance, oral glucose tolerance test

ABSTRACT

Aim: To determine a valid numerical score according to the present risk factors for the prediction of impaired glucose tolerance in our patients.

Materials and Methods: A total of 502 cases (340 females, 162 males; mean age: 48.3 $\pm$ 10.3) without overt diabetes aged over 20, whose fasting plasma glucose level were below 126 mg/dl were included in this study. After fasting blood samples were drawn, a 2-h oral glucose tolerance test was performed. Bivariate and multivariate analyses were performed to obtain a numerical score for predicting impaired glucose tolerance using risk factors such as age, sex, positive family history for diabetes, body mass index, waist circumference, blood pressure, triglycerides, HDL cholesterol, and fasting plasma glucose.

Results: According to the 2-h plasma glucose levels, impaired glucose tolerance was detected in 96 of the patients, and diabetes was detected in 5 patients, while the remaining 401 patients had normal glycaemic values. Age (≥50), hypertension, high triglycerides, large waist, body mass index $\geq$ 25 kg/m^2, and a fasting plasma glucose level of 100-109 mg/dl, or 110-125 mg/dl were associated with an impaired glucose tolerance ($p<0.05$). In a 8-point scale formed using these 6 parameters, a score of $\geq$ 6 could predict impaired glucose tolerance with a specificity of 99% and positive predictive value of 63%.

Conclusion: A numerical score that could be used to predict impaired glucose tolerance in our patients has been proposed with this study.

INTRODUCTION

Diabetes is one of the main causes of mortality and morbidity worldwide. Risk factors such as central obesity, hypertension and dyslipidemia, frequently co-exist in patients with diabetes (1,2). Impaired glucose tolerance (IGT) is an important intermediate step in the natural course of type 2 diabetes (3). Patients with IGT have higher risk for type 2 diabetes and development of cardiovascular disease, therefore; they constitute an important target group in primary prevention (4-6). In this study, the aim was to determine the predictors of positive results for IGT and to find out a valid numerical

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score for prediction of IGT to maximize the yield of oral glucose tolerance test (OGTT) in screening patients.

MATERIALS AND METHODS

The study was performed on patients who are being followed up in Istanbul Goztepe Teaching and Research Hospital, Internal Medicine outpatient clinics and meet the criteria below. Before the study procedure was started, patients' informed consent and local ethical committee approval (approval date and number: 01-06-2004/15) were obtained. Principles of Helsinki Declaration were followed during the study.

The inclusion criteria for the study: Patients at ≥20 years old are included if they have a written informed consent. The exclusion criteria for the study: Known diabetes or fasting plasma glucose ≥ 126 mg/dl, pregnancy, severe liver, heart and renal failure, endocrinologic disorder or any acute disease or surgery in the last three months or cardiovascular event, inactivity for a long period of time or rigorous exercise, severe hypoglycemic attacks or use of medicine effecting carbohydrate metabolism such as steroids, diuretics, oral contraceptives, diphenylhydantoine, thyroxine, beta blockers, or nicotinic acid for the last week.

In eligible patients, that were willing to participate in the study, OGTT with 75 g glucose was performed, after fasting venous blood samples were drawn. IGT was defined as the 2-h plasma glucose levels between 140 and 199 mg/dl (7). Bivariate and multivariate analyses were performed to obtain a numerical score for predicting IGT, using fasting plasma glucose, triglycerides, high-density lipoprotein (HDL) cholesterol, blood pressure, body mass index (BMI), waist circumference, age, sex, and positive family history for diabetes.

The World Health Organization protocol was applied for the OGTT (8). For the metabolic syndrome parameters, the diagnostic criteria suggested by the American National Cholesterol Education Program, Adult III Treatment Panel (NCEP-ATP III) was used (blood pressure ≥130/85 mmHg (or antihypertensive medication); fasting plasma glucose ≥110 mg/dl (or antidiabetic medication); fasting triglycerides ≥150 mg/dl; HDL cholesterol <40 mg/dl (male), or <50 mg/dl (female); waist circumference >102 cm (male), or >88 cm (female)) (9).

To determine plasma glucose and lipid levels, venous blood samples taken into dry tubes were centrifuged immediately, and measurements were carried out in an Olympus 5223 autoanalyzer. Enzymatic methods were used for glucose and triglycerides, and direct methods were used for HDL cholesterol. Blood pressures were measured after at least 5 minutes of rest in the sitting position in both arms with a proper mercury manometer taking the Phase I and Phase IV Korotkoff sounds as the basis. Systolic and diastolic blood pressures were noted with an interval of at least 3 minutes in between two measurements. Body mass index was calculated using the Quetlet index (weight/height: kg/m^2). Those cases with a BMI ≥30 kg/m^2 were considered obese, while those with a BMI between 25 and 29.9 kg/m^2 were considered overweight (10). The waist circumference of patients were measured by using a measuring tape positioned at the high point of the iliac crest. The measurement was made at minimal respiration to the nearest 0.1 cm, with the tape snug but not compressing the skin. For positive family history for diabetes, diabetes had to be present in one of the first degree relatives.

Statistical analyses were carried out using the NCSS McGraw Hill program pack. Besides the descriptive statistics (mean, standard deviation), in the comparison of qualitative data, chi square test were used. Odds ratios (OR) were calculated for qualitative data, and using logistic regression analysis, risks for all the variables with 95% confidence interval (CI) were determined. After logistic regression analysis, a risk scoring was performed taking the higher limits of the 95% CI into consideration. According to the OGTT result, the sensitivity, specificity, positive and negative predictive values of this risk score, and relative risk and the accuracy of the test were calculated. The results were evaluated in 95% CI with a p value of less than 0.05 for statistical significance.

RESULTS

The study was carried out on a total of 502 patients (340 females, 162 males) over 20 years of age (mean age: 48,3 ± 10.3). According to the 2-h plasma glucose levels, IGT was detected in 96 of the patients, and diabetes was detected in 5 patients, while the remaining 401 patients had normal glycaemic values.

In bivariate analysis, IGT was found to be related to age (50-59, or ≥60), female sex, positive family history for diabetes, BMI (25-29.9, or ≥30 kg/m^2), waist circumference (male >102 cm, female >88 cm), blood pressure (systolic ≥130 mmHg, diastolic ≥85 mmHg), triglycerides level (≥150 mg/dl) and fasting plasma glucose level (100-109 mg/dl, or 110-125 mg/dl), ($p<0.05$) (Table 1).

Table 1. Bivariate analysis of impaired glucose tolerance.

		IGT (+)		IGT (-)		
Sex	female	77	80.2%	263	64.8%	χ^2:8.45
	male	19	19.8%	143	35.2%	p=0.004
Age (year)	≤49	22	22.9%	241	59.4%	
	50-59	54	56,3%	144	35,5%	χ^2:40.19
	≥60	20	20.8%	21	5.2%	p=0.0001
Family history for diabetes	(+)	41	42.7%	123	30.3%	χ^2:5.43
	(-)	55	57.3%	283	69.7%	p=0.02
Body mass index (kg/m2)	<25	9	9.4%	149	36.7%	
	25-29.9	39	40.6%	167	41.1%	χ^2:31.83
	≥30	48	50.0%	90	22.2%	p=0.004
Waist circumference (cm)	female >88 male >102	72	75.0%	209	51.5%	χ^2:17.43
	female ≤88 male ≤102	24	25.0%	197	48.5%	p=0.0001
Blood pressure (mmHg) (systolic, diastolic)	≥130, ≥85	56	58.3%	157	38.7%	χ^2:12.29
	<130, <85	40	41.7%	249	61.3%	p=0.0001
Triglycerides (mg/dl)	≥150	57	59.4%	123	30.3%	χ^2:28.54
	<150	39	40.6%	283	69.7%	p=0.0001
HDL cholesterol (mg/dl)	female ≥50 male ≥40	46	47.9%	176	43.3%	χ^2:0.657
	female <50 male <40	50	52.1%	230	56.7%	p=0.418
Fasting plasma glucose (mg/dl)	<100	26	27.1%	254	62.6%	
	100-109	38	39.6%	115	28.3%	χ^2:53.88
	110-125	32	33.3%	37	9.1%	p=0.0001

IGT; impaired glucose tolerance, HDL; high density lipoprotein

In multivariate logistic regression analysis, age (50-59, or ≥60, OR: 1.88 (%95 CI: 0.88-4.01), p<0.05 and OR: 5.64 (%95 CI: 2.49-12.78), p<0.05, respectively), BMI (25-29.9 kg/m^{2,} or ≥30 kg/m^{2,} OR: 1.78 (%95 CI: 1.02-3.09), p<0.05 and OR: 4.41 (%95 CI: 1.93-9.06), p<0.05, respectively), waist circumference (female >88 cm and male >102 cm, OR: 1.84 (%95 CI: 0.81-4.16), p<0.05), blood pressure (systolic ≥130 mmHg, diastolic ≥85 mmHg, OR: 1.31 (%95 CI: 0.72-2.40), p<0.05), triglycerides (≥150 mg/dl, OR: 1.41 (%95 CI: 0.88-2.66), p<0.05) and fasting plasma glucose (100-109 mg/dl, or 110-125 mg/dl; OR: 1.82 (%95 CI: 0.92-3.59), p<0.05, and OR: 4.96 (%95 CI: 2.50-9.82), p<0.05, respectively) were found to be associated with IGT (Table 2).

In multivariate logistic regression analyses, a 8-point scale was formed using these parameters that were associated with IGT (Table 3). According to this scoring system, a score of ≤ 2 had a sensitivity of 91% and a negative predictive value of 96% in predicting IGT, whereas a score of ≥ 6 had a specificity of 99% and a positive predictive value of 63% in predicting IGT (Table 4).

DISCUSSION

In this study, predictors of IGT were advanced age, obesity, high triglycerides levels, hypertension and impaired fasting glycemia. Based on this results, we developed 8-point numerical scoring system for predicting IGT to allow clinicians to screen patients first clinically in order to target the population.

Nelson et al (11), developed a numerical score for predicting IGT using risk factors in a study that 2746 cases aged between 40 and 74 had been analyzed, who had underwent OGTT. In that study, fasting plasma glucose levels between 101 and 109 mg/dl, or 110 and 125 mg/dl, obesity (BMI ≥30 kg/m^2), an ethnic origin of Mexican-American background, age between 60 and 74 years, hypertension, and elevated triglycerides levels (≥150 mg/dl) had been found to be associated with IGT, and using these data, an 8-point scale to predict IGT was developed. A score of <2 had a sensitivity of 86% in predicting IGT, whereas a score ≥6 had a specificity of 97%. As a result it was suggested that OGTT should be performed in high-risk patients

Table 2. Multivariate logistic regression analysis of impaired glucose tolerance

		Clinical Model	Logistic Model
		OR (%95 CI)	OR (%95 CI)
Sex	male		
	female	2.20 (1.28-3.78)*	0.43 (0.21-0.85)
Age (year)	≤49		
	50-59	2.33 (1.49-3.67)*	1.88 (0.88-4.01)*
	≥60	4.82 (2.49-9.33)*	5.64 (2.49-12.78)*
Family history for diabetes	(-)		
	(+)	1.71 (1.08-2.70)	0.49 (0.28-0.85)
Body mass index (kg/m2)	<25		
	25-29.9	0.97 (0.62-1.54)	1.78 (1.02-3.09)*
	≥30	3.51 (2.20-5.58)*	4.41 (1.93-9.06)*
Waist circumference (cm)	female ≤88 male ≤102 female >88 male >102	2.82 (1.71-4.66)*	1.84 (0.81-4.16)*
Blood pressure (mmHg) (systolic, diastolic)	<130, <85		
	≥130, ≥85	2.20 (1.41-3.49)*	1.31 (0.72-2.40)*
Triglycerides (mg/dl)	<150		
	≥150	3.36 (2.12-5.32)*	1.41 (0.88-2.66)*
HDL cholesterol (mg/dl)	female ≥50 male ≥40 female <50 male <40	1.20 (0.76-1.87)	0.66 (0.38-1.15)
Fasting plasma glucose (mg/dl)	<100		
	100-119	1.65 (1.04-2.63)	1.82 (0.92-3.59)*
	110-125	4.98 (2.89-8.57)*	4.96 (2.50-9.82)*

OR; odds ratio, HDL; high density lipoprotein

Table 3. Clinical score

		Points
Age (year)	50-59	1
	≥60	2
Body mass index (kg/m2)	25-29.9	1
	≥30	2
Waist circumference (cm)	female > 88 male > 102	1
Triglycerides (mg/dl)	≥150	1
Blood pressure (mmHg) (systolic, diastolic)	≥130 , ≥85	1
Fasting plasma glucose (mg/dl)	100-109	1
	110-125	2
Maximum score		**8**

Table 4. Scoring system aiming to predict impaired glucose tolerance

Score (8)	Sensitivity	Specificity	PPV	NPV	Accuracy	RR	LR(+)	LR(-)
0	0.99	0.17	0.22	0.99	0.86	15.14	1.19	0.06
1	0.96	0.34	0.25	0.97	0.72	8.98	1.45	0.12
2	0.91	0.54	0.32	0.96	0.55	7.98	1.96	0.17
3	0.75	0.73	0.40	0.93	0.36	5.27	2.77	0.34
4	0.59	0.85	0.49	0.90	0.23	4.81	4.02	0.48
5	0.29	0.94	0.52	0.85	0.11	3.42	4.55	0.76
6	0.10	0.99	0.63	0.82	0.03	3.53	7.05	0.91
7	0.01	1.00	0.33	0.81	0.01	1.75	2.11	0.99

PPV; positive predictive value, NPV; negative predictive value, RR; relative risk, LR; likelihood ratio

with scores ≥6. James MB et al (12) analysed the four epidemiological trials (the Framingham Offspring, San Antonio Heart, Mexico City Diabetes, and Insulin Resistance Atherosclerosis Studies) and reported that nonglycemic MetS characteristics such as large waist and high triglycerides in patients with OGTT testing predicted the BGT efficiently.

In multivariety logistic regression analyses of 502 cases who had OGTT and over 20 years of age, it is found that over 50 years of age, large waist, BMI≥25 kg/m², hypertension, high triglycerides levels and impaired fasting glycemia are related to IGT. These results show similarity to the findings of Nelson et al. However in that study there was a relation between IGT and the cases who were between 60 and 74 years and BMI≥30 kg/m², in our study there was a relation between IGT and the patients who were 50 years old or over, large waist and BMI≥25 kg/m². When the metabolic syndrome parameters are considered, the relation between large waist, high triglycerides levels and IGT seems to be similar to data in James MR et. al. study. However in our trial it is found to be different that there is a relationship between high blood pressure and IGT.

In this study a score of maximum 8 points which will predict IGT was obtained. Scoring number which is ≥6 showed 99% specificity and 63% positive predictive value. According to these data, OGTT should be performed in high-risk patients with scoring number ≥6. Negative predictive value was 96% where scoring number was ≤ 2. OGTT as a scanning test is not recommended to low risk group for IGT. An approach which takes other clinical data into consideration in group with scoring number between 2 and 6 is appropriate. In this study one of the characteristics which is important to point out is that in patients with a normal fasting glycemia if there are other risk factors, scoring number may increase to ≥ 6 and there is a possibility for IGT to be detected. For example, in a patient over 60 years of age who has a large waist, high triglyceride levels, BMI≥30 kg/m² and hypertension, the score is 7 and even he is normoglycemic he is included in the high risk group for IGT.

In conclusion, this scoring system could be suggested as an objective criterion to choose which patients should receive OGTT.

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