IMPACT OF THE NEW DIAGNOSTIC CRITERIA ON THE PREVALENCE OF PATHOGLYCEMIC STATUS

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Abstract

Objective: *This study aims to establish the impact of the diagnostic criteria on the prevalence of different pathoglycemic status (diabetes mellitus, impaired glucose tolerance, impaired fasting glucose and the combination of the latter) as well as the assessment of the glycemic status in the general population of the Timis county.* ***Subjects and method:*** *This study was conducted in two groups of subjects from Timisoara:* ***group A*** *which included 833 subjects, of which 364 males (43.7%) and 469 females (56.%) aged 46.9 ± 12.8 (18-79) years who underwent the oral glucose tolerance test and* ***group B*** *including 530 subjects, 262 males (49.4%) and 268 females (50.6%) aged 50 ± 13.7 (18-77) years, who also underwent the oral glucose tolerance test between 1990-1996 for the early detection of diabetes mellitus. The only criterion for the inclusion in the study was that none of the subjects had been previously clearly diagnosed with diabetes mellitus or other disorder of the carbohydrate metabolism.* ***Results:*** *In group A, the prevalence of pathoglycemic status, according to the present recommendations for the diagnosis of diabetes mellitus (WHO 1999), was 28.2% and after the WHO criteria from 1985, 22.9%. In group B, according to the WHO criteria from 1999 the prevalence of pathoglycemic states was 18.5% and after the WHO criteria from 1985, 10.5%.* ***Conclusions:*** *The replacement of the diagnostic criteria from 1985 with those from 1999 resulted in the increase of the pathoglycemic status, especially for diabetes mellitus, through the lowering of the fasting glycemia value used as threshold for its diagnosis, from 140 mg% to 126 mg%. According to the data presented, taking into account the same interpretation criteria (WHO 1999), the prevalence of diabetes mellitus increased from 6% in the period 1990-1996, to 9.1% at present.*

Key words: *pathoglycemic status, diabetes mellitus, impaired glucose tolerance, impaired fasting glucose, prevalence.*

Introduction

The main objective of this study was the determination of the impact of the diagnostic criteria of diabetes mellitus (DM) and of other pathoglycemic categories in Timisoara (Romania) on their prevalence and, secondly, the assessment of the pathoglycemic status (PGS) prevalence according to the current diagnostic criteria (WHO 1999) within the same demographic area.

The PGS includes DM, impaired glucose tolerance (IGT) and, from 1999, impaired fasting glucose (IFG) and the combination IGT+IFG.

A major achievement of the last decades has been the adoption by WHO of some worldwide generally valid criteria, which led to identical interpretations of data which could thus be compared among them. The WHO criteria from 1985 were used until 1999, when two modifications have been made: the

lowering of the fasting glycemia value, from 140 mg% to 126 mg% as threshold diagnosis for DM and the introduction of the IFG category (4,12).

The IFG category has been introduced to draw our attention on the importance of the increase of the fasting glycemia between 110-125 mg%, as cardiovascular risk factor for the occurrence of DM as well as for the early setting up of prevention measures (1,2).

Subjects and method

Group A included 833 subjects, 364 males (43.7%) and 469 females (56.3%), aged 46.9 ± 12.8 (18-79) years, investigated between 2005-2007 and recruited from five trading companies from Timisoara. The sole criterion for the inclusion in the study was that none of the subjects had been previously diagnosed with DM or with other disorder of the carbohydrate metabolism.

All these persons underwent the oral glucose tolerance test (OGTT), interpreted after the WHO criteria from 1985 and after those from 1999 as well.

Group B included 530 subjects, 262 males (49.4%) and 268 females (50.6%) aged 50 ± 13,7 (18-77) years, who underwent OGTT between 1990-1996 for the early detection of DM. In this group the prevalence of DM and of other disorders of the carbohydrate metabolism (IGT, IFG, IGT+IFG) was analysed retrospectively. In the two groups, glycemia was measured with the enzymatic glucose-oxidase method.

The two groups were organised in a database created in Microsoft Excel, in the form of files. The statistical analysis of the data was performed by means of a computer, on files created with the specialized programs: EPI 3.2.2 and OpenEpi. This analysis consisted of: 1. the calculation of the frequency of the percentages for the qualitative variables; 2. the calculation of the arithmetic averages and of the standard deviations for quantitative variables; 3. the statistical comparison between group means and the tests:● *unpaired* Student's *t-test* and *paired* Student's *t-test* – two samples; ● *ANOVA (ANalysis Of VAriance - "variance analysis")*- several samples; 4. statistical comparison of the percentages with the chi-square test (χ^2 test); 5. calculation of the correlation coefficient Pearson - r with the interpretation proposed by Colton; 6. obtainment of the regression right; 7. the statistical assessment of the results was carried out using the decision criterion of the statistical tests.

Results

In ***group A,*** according to 1999 WHO diagnostic criteria, out of the 833 cases, 235 persons (28.2%) had PGS. Would the 1985 criteria have been applied, the percentage of the cases with PGS would have been 22.9% (Table 1). The difference is explained by the lowering of the fasting glycemia value used as „threshold" for the diagnosis of DM, from 140 mg% to 126 mg% and by the introduction in the classification of the IFG category. Some subjects had IFG and IGT as well.

Table 1. PGS prevalence using different methods of diagnostic criteria, in group A

Pathoglycemic category	1985	1999
	Percent (%)	Percent (%)
DM	8.3	9.1
IGT	14.6	7.9
IFG	-	5.3
IFG +IGT	-	59
Total	22.9	28.2
Statistic semnification	p<0.001	

Table 2. PGS prevalence using different sets of diagnostic criteria, in group B

Patho-glycemic category	1985	1999
	Percent (%)	Percent (%)
DM	4.5	6
IGT	6	4.5
IFG	-	3
IFG+IGT	-	4.9
Total	10.5	18.5
Statistic semnification	p<0.001	

Significant differences are to be noted in above-mentioned data (p<0.001, ES) with regard to the proportion of pathoglycemic persons, subject to the diagnostic criteria used.

In group A, according to the WHO criteria from 1985, some subjects would have been classified as normal glycemic but, by the introduction of IFG and by the lowering of the fasting glycemia, they are being classified in the pathoglycemic category.

According to the present diagnostic criteria, the prevalence of DM increased from 6%, ten years ago, to 9.1% at present (p<0.001). Even using the criteria from 1985, the actual prevalence of DM increased from 4.5% to 8.3% (p<0.001) (Figure 1).

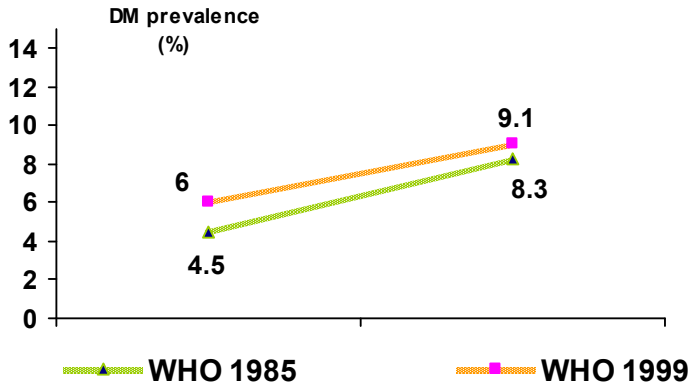

Figure 1. DM prevalence at present as compared with the period 1990-1996, subject to the diagnostic criteria used

As concerning IGT, its prevalence did not change significantly. If in group A, according to the WHO criteria from 1985, the IGT prevalence was 14.6%, after the criteria from 1999 it was 13.8% (5.9% had both IGT and IFG). In group B, according to the WHO criteria from 1985, the IGT prevalence was 6% and based on the criteria from 1999, 9.4% (4.9% had both IGT and IFG). In the meantime, regardless of the criteria used, IGT prevalence increased from 6%, ten years ago, to 14.6% at present, according to WHO criteria from 1985 and from 9.4% to 13.8% according to WHO criteria from 1999 ($p<0.001$) (Figure 2).

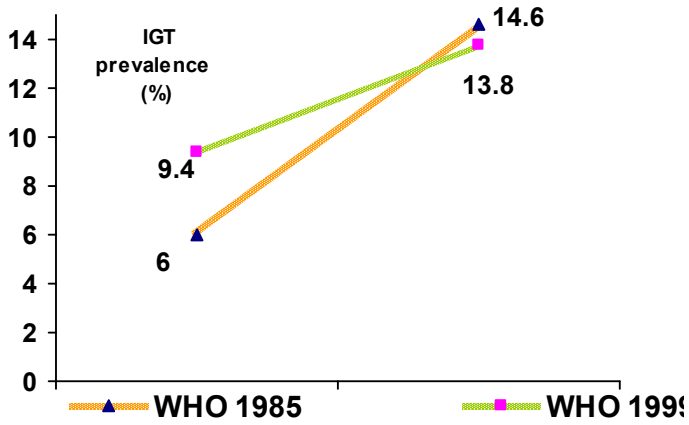

Figure 2. IGT prevalence ten years ago and at present, subject to the diagnostic criteria used

It is well known that the fasting glycemia and the glycemia at 2 hrs. are not detecting the same subjects with DM. In group A, the fasting glycemia test detected 55.3% persons with DM and the 2 hrs. glycemia test, 75%. In group B, the fasting glycemia test detected 31.3% persons with DM and the glycemia at 2 hrs. test detected 68.7% persons (Table 3).

Table 3. Fasting glycemia versus glycemia at 2 hours, aiming to detect as many persons with DM as possible

Category	Group A	Group B
	Percent (%)	Percent (%)
Fasting glycemia ≥126 mg%+ glycemia at 2 hrs. <200 mg%	25	18.7
Fasting glycemia ≥126 mg%+ glycemia at 2 hrs.≥200 mg%	30.3	12.5
Fasting glycemia <126 mg%+ glycemia at 2 hrs.≥200 mg%	44.7	56.2

We notice that in group A, from those who met the 2 hours criterion, 44.7% did not meet the fasting glycemia criterion as well, and 25% from those detected based on the fasting glycemia, did not meet the 2 hours criterion. In group B, only 12.5% met both criteria.

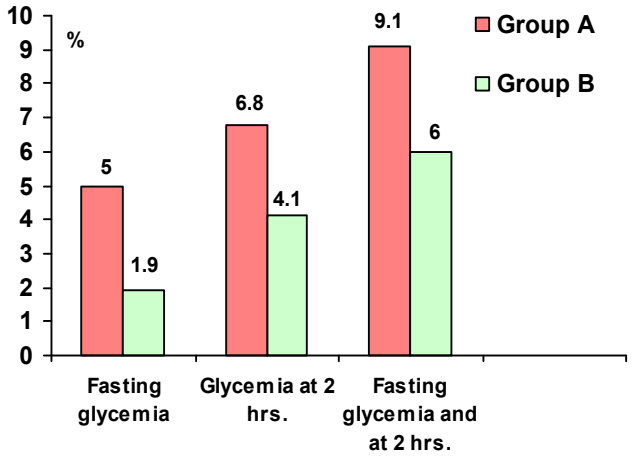

Figure 3. Prevalence of DM subject to the method used in the two groups

In relation to the *diagnostic criteria of DM*, we obtained following data in the study population:

- ***group A***: using *only* the fasting glycemia and the value of 126 mg% as a diagnosis „threshold", a number of 42 persons would have been diagnosed with DM and its prevalence would have been 5%; using *only* the 2 hours glycemia, 57 persons (6.8%) would have been considered diabetic (2 h glycemia ≥200 mg%); 76 persons (9.1%) were diagnosed with DM using the fasting glycemia and the glycemia at 2 hours as well.
- ***group B*: *only*** by means of the fasting glycemia, 10 persons (1.9%) were diagnosed with DM; *only* by means of the 2 hours glycemia, 22 persons (4.1%) were diagnosed with DM and using both methods, 32 persons (6%) (Figure 3).

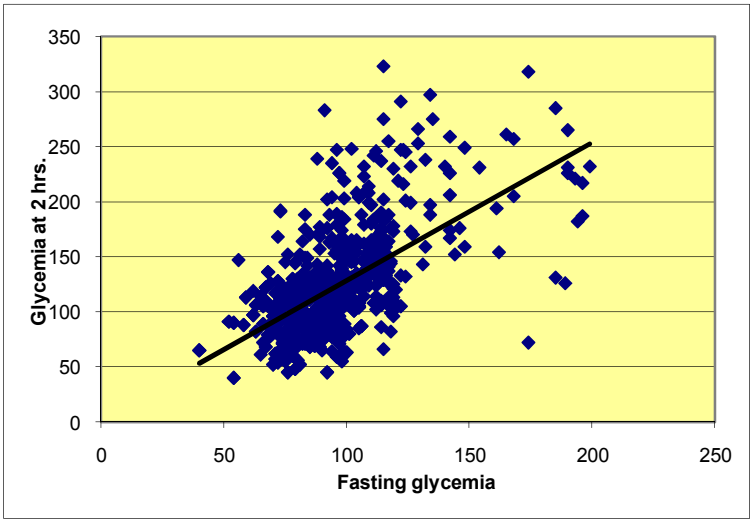

Figure 4. Correlation between fasting glycemia - glycemia at 2 hrs. (r=0.06, p<0.001)

Observing the correlation between the fasting glycemia and the glycemia at 2 hrs., a moderate to strong direct correlation (r=0,06, p<0.001) has been noted between the two values (Figure 4).

Discussions

The modification of the diagnostic criteria of a disease always influences the prevalence of such disease. This truth was also expected in the case of DM and of other PGSs as well, but the size of this impact cannot be estimated from the outset (9,10,11).

The WHO criteria from 1999 bring two new modifications as compared with those from 1985, namely: the decrease of the lowest value of the fasting glycemia used for the diagnosis of DM (from 140 mg% to 126 mg%) and the inclusion of a new pathoglycemic category, that of impaired fasting glycemia, which may be translated in Romanian as the alteration or modification of the fasting glycemia, named sometimes as basal glycemia, a rather unclear notion (13,16).

The lowering of the fasting glycemia from 140 mg% to 126 mg% resulted in an increase of the subjects which could be classified within the DM category and IFG extended the area of intermediate disorders of glucose regulations, joining IGT.

Our data show that with the decrease of the fasting glycemia from 140 mg% to 126 mg% and with the introduction of the IFG category, the percentage of pathoglycemic subjects increased from 22.9% to 28.2% in group A and from 10.5% to 18.5% in group B and the prevalence of DM increased from 8.3% to 9,1% in group A and from 4.5% to 6% in group B.

We know now that the fasting glycemia sets the diagnosis of DM in some subjects and the glycemia at 2 hours by means of OGTT in other subjects, however there exists a third category which can be diagnosed by means of both methods (7,14).

In the study population, we have noticed differences concerning the prevalence of DM, subject to the diagnostic method used. Applying only the fasting glycemia, the prevalence of DM was 5% in group A and 1.9% in group B. Measuring the 2 hours value during OGTT, the prevalence of DM was 6.8% in group A and 4.1% in group B. By means of both diagnostic methods, the DM prevalence was 9.1% in group A and 6% in group B. Similar results have been reported in a study performed in Finland (8).

Resnick, Harris and Davies suggest that the diagnosis of DM during OGTT should not be based only on the fasting glycemia but on the glycemia at 2 hours as well (15).

Using *only* the fasting glycemia for the diagnosis of DM, the relative sensitivity of the method was 55.3% in group A and 31.3% in group B. Using *only* the glycemia at 2 hours, the sensitivity of the method increased to 75% in group A and to 68.7% in group B.

In the DECODE European study, out of 1517 persons detected with DM, only 28% met both diagnostic criteria. From the study group, 40% were diagnosed using the fasting glycemia and 31% using the glycemia at 2 hours during OGTT. From those who met the 2 hours criteria, 51% have not met the criterion for the fasting glycemia and 59% of those detected based on the fasting glycemia, have not met the 2 hours criterion.

In the NHANES III study, out of the subjects without any previous history of DM, aged between 40 and 74 years, 44% met both diagnostic criteria, 14% were detected only

based on the fasting glycemia and 41% were detected only based on the glycemia at 2 hours during OGTT.

The discrepancy between the European and the US population can be explained by the fact that obesity is much more frequent in the US and it seems to be combined with higher values of fasting glycemia. Furthermore, the NHANES study did not include persons aged over 75 years, who seem to show higher values of 2 hours glycemia. Similar results have been observed in the San Antonio Group and the Paris Prospective Study (3,6).

In the epidemiologic studies, the measurement of the fasting glycemia is sufficient as it diagnoses two of PGSs (DM and IFG), but for the safety of the DM diagnosis in the clinical cases encountered in the medical practice, OGTT plays an essential role.

The predictive value of the 2 hours glycemia during OGTT seems to be higher in macrovascular complications and cardiovascular mortality than in the fasting glycemia, although in microvascular complications the two values seem to be similarly predictive (17,18,19).

Conclusions

The WHO criteria from 1999 for the diagnosis of DM determine a significant increase of the prevalence of impaired glucose regulations as compared with those from 1985.

Although both OGTT and the fasting glycemia are been used in the clinical practice, the fasting glycemia is strongly recommended in the epidemiologic studies, as a test which can be performed easier, more quickly, more convenient and more ready to be accepted by the patient and cheaper at the same time.

However, OGTT offers some obvious advantages as both fasting glycemia and the glycemia at 2 hours are being measured and this test is preferred for the diagnosis of DM when the fasting glycemia is under 126 mg%, especially if the subject shows a higher theoretical risk to be diabetic.

Measuring only the fasting glycemia, one cannot detect individuals with IGT and by the glycemia at 2 hours, the ones with IFG. The concomitance between the two tests is extremely useful.

REFERENCES

1. American Diabetes Association Expert Committee. Report of the Expert Committee on the Diagnosis and Clasification of Diabetes Mellitus. Diabetes Care, 1997; 20: 1183.

2. American Diabetes Association: Standards of medical care for patients with diabetes mellitus. Diabetes Care, 2003; 26 (Suppl. 1): S33–S50.

3. Balkau B, Forhan A, Eschwege E. Two hour plasma glucose is not unequivocally predictive for early death in men with impaired fasting glucose: more results from the Paris Prospective Study. Diabetologia, 2002; 45: 1224–1230.

4. Bennett PH. Impact of the new WHO classification and diagnostic criteria. Diab, Obesity and Metab 1999; 1(Suppl 2): S1-S6.

5. Burke JP, Haffner SM, Gaskill SP, Williams KL, Stern MP: Reversion from type 2 diabetes to nondiabetic status: influence of the 1997 American Diabetes Association criteria. Diabetes Care, 1998; 21: 1266–1270.

6. Burke JP, Williams K, Haffner SM, Villalpando CG, Stern MP: Elevated incidence of type 2 diabetes in San Antonio, Texas, compared with that of Mexico City, Mexico. Diabetes Care, 2001; 24:1573–1578.

7. Davies MJ, Raymond NT, Day JL, Hales CN, Burden AC. Impaired glucose tolerance and the fasting hyperglycaemia have different characteristics. Diabet Med, 2000; 17: 433–440.

8. de Vegt F, Dekker JM, Ruhe HG, Stehouwer CD, Nijpels G, Bouter LM, Heine RJ. Hyperglycaemia is associated with all-cause and cardiovascular mortality in the Hoorn population: the Hoorn Study. Diabetologia, 1999; 42: 926–931.

9. Expert Committee on the Diagnosis and a Classiffication of Diabetes Mellitus. Report of the expert committee on the diagnosis and classiffication of the diabetes mellitus. Diabetes Care, 1997; 20: 1183-1197.

10. Expert Committee on the Diagnosis and Classification. Follow-up Report on the Diagnosis of Diabetes Mellitus. Clin. Diabetes, 2004; 22: 71-79.

11. Expert Committee on the screening of Diabetes Mellitus. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care, 2005; vol: 28 Suppl. 24.

12. Gabir M, Hanson RL, Debelea D, Imperatore G, Rousmain J, Bennett PH, Knowler WC: Plasma glucose and prediction of microvascular disease and mortality: evaluation of 1997 American Diabetes Association and 1999 World Health Organization criteria for diagnosis of diabetes. Diabetes Care, 2000; 23: 1113–1118.

13. McCance D, Hanson RL, Pettitt DL, Bennett PH, Hadden DR, Knowler WC. Diagnosing diabetes mellitus—do we need new criteria? Diabetologia, 1997; 40: 247–255.

14. McCance DR, Hanson RL, Charles MA, Jacobsson LT, Pettitt DJ, Bennett PH, et al. Which test for diagnosing diabetes? Diabetes Care 1995; 18: 1042-1044.

15. Resnick HE, Harris TB, Harris T, Cook D, Cappuccio FP, Davies M, Wiener K, Roberts NB, Famuyiwa O, Borch-Johnsen K, Tuomilehto J, Qiao Q, Balkau B. New diagnostic criteria for diabetes mellitus. BMJ, 1999; 318: 531-531.

16. Shaw JE, Zimmet PZ, Hodge AM, de Courten M, Dowse GK, Chitson P, Tuomilehto J, Alberti KGMM: Impaired fasting glucose: how low should it go? Diabetes Care, 2000; 23: 34–39.

17. Stern MP, Fatehi P, Williams K, Haffner SM. Predicting future cardiovascular disease: do we need the oral glucose tolerance test? Diabetes Care, 2002; 25: 1851–1856.

18. Stern MP, Williams K, Haffner SM: Identification of persons at high risk for type 2 diabetes mellitus: do we need the oral glucose tolerance test? Ann Intern Med, 2002; 136: 575–581.

19. Tai ES, Goh SY, Lee JJM, Wong MS, et al. Lowering the Criterion for Impaired Fasting Glucose: Impact on disease prevalence and associated risk of diabetes and ischemic heart disease. Diabetes Care, 2004; 27: 17