EPIDEMIOLOGICAL CHARACTERISTICS OF DIABETES MELLITUS AND IMPAIRED GLUCOSE REGULATION IN THE POPULATION OF HUNEDOARA COUNTY

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Abstract

There are few studies that have examined the prevalence of type 2 diabetes mellitus (DM) in Romania. In the study described in this paper we evaluated the utility of HbA1C in the screening and diagnosis of type 2 DM, in the general population of Hunedoara County, and determined the prevalence of type 2 DM in this area of the country. A cross-sectional study was conducted, that included 505 subjects. Type 2 DM was found in 81 persons (16.03%) and an area of 0.717 (95% CI 0.668 - 0.766) under the ROC curve was found for HbA1C as a predictor of type 2 DM, when FPG≥110mg/dl.

key words*: Type 2 DM epidemiology, HbA1C, glucose tolerance*

Introduction

Type 2 diabetes mellitus (type 2 DM) is an important public health problem across the world, because of its serious complications and health consequences. The prevalence is growing, together with the increasing rate of obesity. There are few studies that have examined the prevalence of type 2 DM in Romania. The disease is often asymptomatic at the onset and can remain undiagnosed for some years. Some papers showed that, even in more developed countries, approx. 50% of cases remain undiagnosed [1].

The oral glucose tolerance test (OGTT) has traditionally been used to classify the status of glucose tolerance for the diagnostic, considering this as the "golden standard". More recently, glicated haemoglobin (HbA_{1C}) has been considered to be a practical alternative for screening because it is more convenient and easier to reproduce, but optimal cut offs are still in debate [2-9].

In 2010, according to the Romanian National Statistics Institute, Hunedoara County has 463,102 inhabitants [10]. At the end of June 2010, 20,592 patients were registered with DM. The crude prevalence of type 2 DM increased in the last 8 years: from 2.07% in 2002, to 4.45% in 2010.

In this study, we aimed at evaluating the utility of HbA_{1C} for the screening and diagnosis of type 2 diabetes mellitus, defined by oral glucose tolerance testing, in the general population of Hunedoara County. At the same time, our study described the epidemiological characteristics of DM in Hunedoara County and determined the current prevalence of type 2 DM in this area of the country.

Material and method

The study was designed as a cross-sectional investigation and was based on the General Practitioners (GPs) lists of people. We selected 4761 subjects, from all over the county, both from urban and rural areas, and 707 of them were previously diagnosed with DM. Demographical data, anthropometric measurements and a minimum of biochemical parameters were collected. We excluded the persons known to have DM and invited the remaining subjects to take an oral glucose tolerance test (OGTT). However, only 505 of them accepted to undergo the test.

The 505 subjects were instructed to fast minimum 8 hours overnight before examination. After the blood sample for fasting plasma glucose (FPG) and HbA1C was obtained (by venous-puncture), 75g of monohydrate glucose solutions were ingested. Blood samples for glucose concentrations were obtained at 60 and 120 minutes after ingestion. All specimens were analyzed at *Bioclinica Laboratory Deva*. HbA_{1C} was determined by Meia method (Abbott) on Axsym analyzer using for standardization NGSP/DCCT %, and glycemia was determined using hexokinase method on Architect analyzer. Anthropometric measurements were undertaken: standing height was measured using a fixed stadiometer with a parallel crane to the floor and the body weight was measured on a classical mechanical scale. Waist circumference was measured at the mid-way between the lower rib margin and the iliac crest, with an unstretched tape. The participants were instructed to wear light clothing and breathe gently during the measurements. BMI was calculated as weight [kg] divided by the square of height [m].

Statistical analysis was performed using SPSS v. 15.0. The results for continuous variables were expressed as mean values, standard deviations, and ranges. The t-test for independent samples was applied to test the statistical significance of differences observed between the values for the two sexes (i.e. females and males). For investigating the predictive value of HbA_{1C} as a screening instrument, the Receiver Operating Characteristic (ROC) curve was determined, with estimated sensitivity, specificity and Odds Ratios (OR) for different cutoffs values. For the statistical tests and risk estimates, the 0.05 (i.e. 5%) two-tailed level of significance was considered, with a 0.95 (i.e. 95%) confidence interval (CI) around the point estimates.

Results

From the 505 participants, 283 were females and 222 males, 396 were from an urban and 109 from a rural area. The mean age was 56 years, the mean height was 166,18cm, the mean weight was 77,92kg, the mean waist circumference was 96,72cm and the mean BMI=28,16kg/m^2 (Table 1).

Table 1. Descriptive statistics for the parameters investigated in the 505 subjects who were included in the study.

Variable	Total number	Min	Max	Mean +/- std. deviation
HbA1c [%]	505	4.60	12.00	5.94 +/- 0.76
FPG [mg/dl]	505	52	313	107.60 +/-23.82
1hPG [mg/dl]	505	56	468	163.40 +/- 64.21
2hPG [mg/dl]	505	35	467	124.99 +/- 59.33
Height [cm]	505	144	193	166.18 +/- 8.99
Weight [kg]	505	40	150	77.92 +/- 16.52
Waist circumference [cm]	505	62	149	96.72 +/- 13.98
BMI [kg/m^2]	505	17.10	53.78	28.16 +/- 5.33
Waist circumf. [cm] / Height [cm]	505	0.37	0.89	0.58 +/- 0.084
Age [years]	505	16	89	56.19 +/- 13.26

Table 2. Glucose tolerance categories, according to the WHO criteria [1, 3-5].

Glucose tolerance category	Glycemia
NGT	FPG < 110 mg/dl and 2hPG < 140 mg/dl
IFG	FPG 110 - 125 mg/dl and 2hPG < 140 mg/dl
IGT	FPG < 126 mg/dl and 2hPG 140 - 199 mg/dl
IFG + IGT	FPG 110 - 125 mg/dl and 2hPG 140 -199 mg/dl
DM	FPG ≥ 126 mg/dl and/or 2hPG ≥200 mg/dl

Table 3. The distribution of glucose tolerance by categories defined according to the WHO criteria [1, 3-5].

NGT	Isolated IFG	Isolated IGT	IFG+IGT	DM
277 (54.85%)	69 (13.66%)	49 (9.70%)	29 (5.74%)	81 (16.03%)

Based on World Health Organization (WHO) criteria [1, 3-5], individuals were classified into five groups, according FPG and glucose tolerance, as follows: normal glucose tolerance (NGT), isolated impaired fasting glucose tolerance (IFG), isolated impaired glucose tolerance (IGT), combined IFG and IGT and DM (Table 2).

The distribution of glucose tolerance by categories is shown in Table 3.

These numbers show that the crude prevalence of type 2 DM in Hunedoara County could be greater than the actually registered one [10].

Out of 505 persons who underwent the OGTT, 315 (62.37%) had FPG above 100mg/dl, 169 (33.46%) above 110mg/dl, and 62 (12.27%) above 126mg/dl. If we applied the American Diabetes Association criteria and considered any fasting plasma glucose above 100mg/dl as abnormal, then the number of persons who had IFG and IFG+IGT would increase to 182 (36.30%) and 55 (10.89%) respectively, while the number of cases of IGT would decrease to 23 (4.55%).

In Figure 1, we represented the relation between HbA1C and the glucose tolerance of our subjects.

Regarding the values for HbA_{1C}, 77 persons (15.24%) had values above 6.5%, and 150 persons (29.70%) had values between 6.0% and 6.5% (i.e. impaired $HbA_{1C,}$

considered to reflect pre-diabetes). The numbers did not significantly differ from those of DM detected by fasting glycemia and OGTT. However, for impaired glucose tolerance they were smaller than those detected by glycemia.

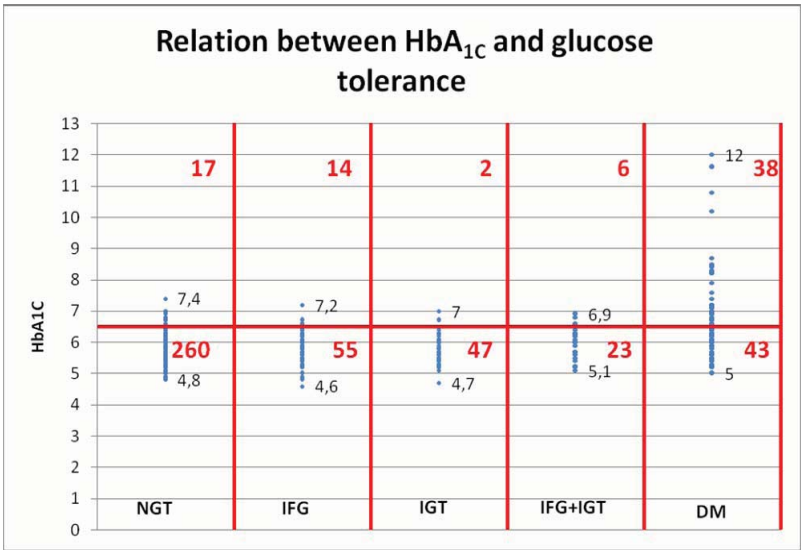

Figure 1. The relationship between HbA_{1C} and glucose tolerance ($HbA_{1C} \geq 6.5\%$).

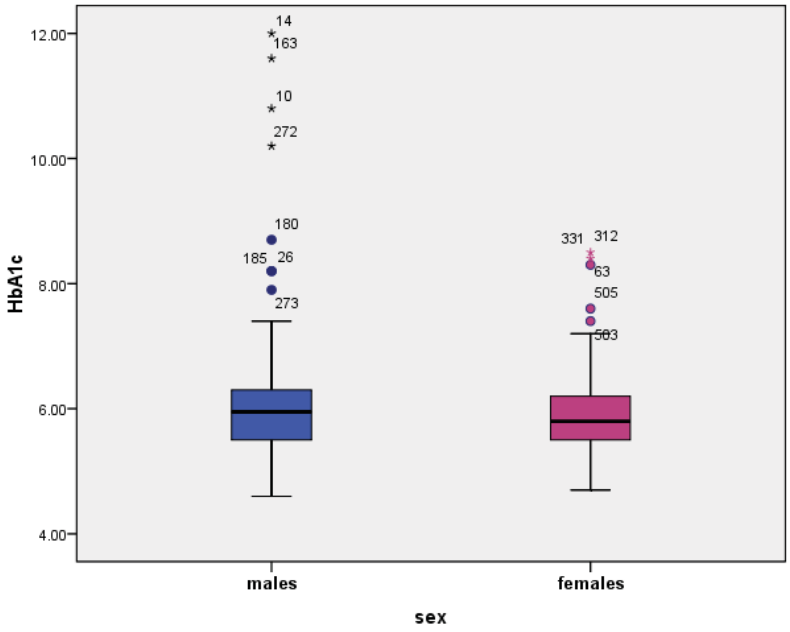

Figure 2. The boxplot representation for the values of HbA1C. The median values, the 25% and 75% quartiles are represented. The t-test for independent samples showed a statistically significant difference (p=0.006) between the values of HbA1C for the two sexes.

We observed a statistically significant difference between the values of HbA1c for the two sexes (Table 4 and Figure 2). However, as we focused on investigating the value of HbA1c as an instrument for screening, we further considered the patients' population as a whole, i.e. both sexes together.

Table 4. Descriptive statistics for HbA1c.
The statistical significance was marked as * for significant results and ** for very significant results.

HbA1c		N	Mean +/- std. deviation	t-test for independent samples
Sex	male	222	6.05 +/- 0.92	Unequal variances (test Levene, p=0.028*). Unpaired t-test (t=2.790, df=352.471) p=0.006**
	female	283	5.86 +/- 0.58	

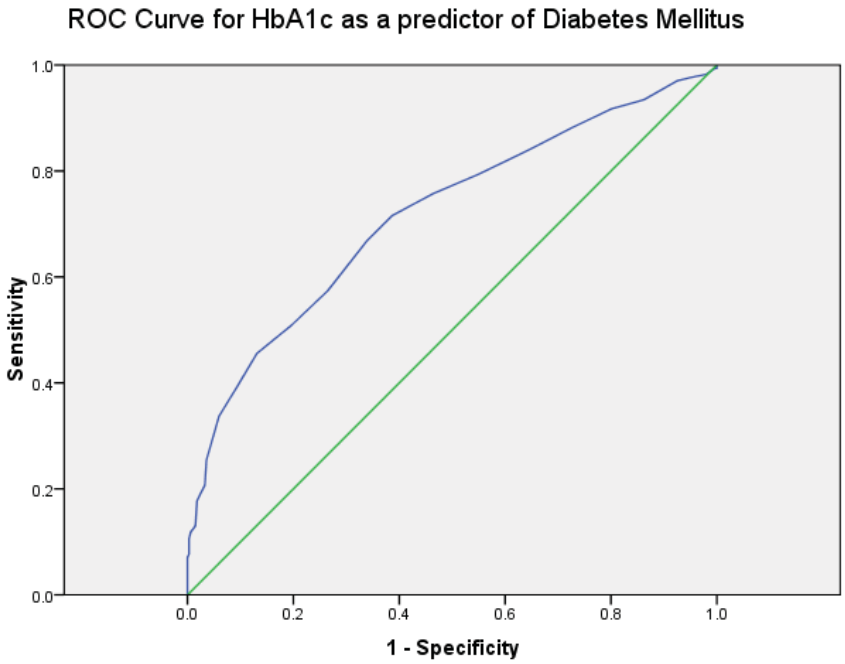

Figure 3. The ROC curve for HbA1c as a predictor for Diabetes Mellitus (the gold standard for positivity was FPG >= 110mg/dl). The area under the curve is 0.717 (95% CI 0.668 - 0.766).

Considering the gold standard for glucose intolerance diagnosis as FPG ≥110mg/dl, we investigated the predictive value of HbA_{1C}. The area under the ROC curve was 0.717 (95% CI 0.668 - 0.766), proving a reasonable quality of classification (Figure 3). For a cut off value of 6.5% , the specificity was 94.05% and sensitivity was 33.76%. The OR was 8.041 (95% CI 4.625 - 13.981). For a cut off value of 6%, the values for specificity and sensitivity, were 66% and 66.86% respectively, while the OR was 3.930 (95% CI 2.655 - 5.815). For smaller cut off values (e.g. 5.7%) the specificity decreased dramatically.

Discussion and conclusions

Our population sample suggested a greater crude prevalence than the registered one. This might be a consequence of the age distribution in the sample, which was not entirely representative for the general population: the mean age of the subjects was 56 years, with a standard deviation of 13.26, although the range varied between 16-89 years. For the diagnosis we used the OGTT, incorporating

FPG, which minimized the possibility of misdiagnosis. At the same time, sampling subjects from all over the county excluded any differences between zones and improved the representativeness of the subjects in the study.

The HbA_{1C} proved to have a reasonable power of prediction of type 2 DM. Moreover, it is more stable than fasting plasma glucose (FPG), does not impose fasting to the patients, and can be determined at any time of the day. On the other hand, it is expensive and the method is not yet standardized in all laboratories of the county. In addition to that, HbA_{1C} is a continuous variable for DM and pre-diabetes, so any chosen cut off values are somewhat arbitrary. Some papers found that single HbA_{1C} cut off values have limited clinical utility in identifying persons with glucose intolerance, therefore recommend two cut off values to rule in or out any alterations of glucose tolerance [11]. In our study, we found 6% as an optimal cut off value for $HbA_{1C,}$ for it had a good specificity and sensitivity, while the recommended cut off value for HbA_{1C} (i.e. $\geq$6.5%) led to a better specificity, but worsened the sensitivity, therefore missing too many positive patients.

Taking all these into account, using FPG for screening would be more cost-effective, as a glycemia test costs 8.5 RON, whereas the HbA_{1C} costs 32 RON. At the same time, we should not underestimate the important disadvantages of the glycemia test: the requirement of previous fasting and of its great variability.

A limitation of this study would be that both FPG and 2 hour post loading glucose were measured only once, while guidelines recommend two separate measurements on two different days to confirm the analysis.

In summary, these data and results show that, for the time being and for our area of the country, it would be better to use the fasting plasma glucose for diagnosing type 2 DM, according to the actual recommendations of WHO for screening purposes [7, 8, 12]. In addition, more studies are needed to assess the real prevalence of DM in our country, focusing more on the groups of people at risk.

Acknowledgements. We would like to kindly thank the General Practitioners, who assisted the authors with their work : Dr. Mircea Artean, Dr. Grigore Crisan, Dr. Claudia Croitoru, Dr. Gabriela Gros, Dr. Lucia Lapusca, Dr. Leonora Leahu, Dr. Angela Molot, Dr. Daniela Munteanu, Dr. Silvia Novac, Dr. Cecilia Prundaru, Dr. Corina Radoi.

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