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MULTIFACTORIAL ANALYSIS OF A GROUP OF PREDIABETES PATIENTS IN TERMS OF CARDIOVASCULAR RISK

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Abstract

Background and Aims*: "Prediabetes" is defined by Impaired Fasting Glucose (IFG) or Impaired Glucose Tolerance (IGT), both states associated with increased risk for diabetes and high cardiovascular (CV) risk. The aim of our study was to investigate a population with prediabetes compared to a group from the general population in respect with the risk for progression to diabetes and CV risk parameters.* ***Materials and Methods****: We investigated 124 ambulatory patients with prediabetes and 98 persons without any known metabolic disorders (control group), for CV risk parameters and risk of developing diabetes.* ***Results****: We found statistically significant differences (p <0.05) for average weight, waist, BMI and lipids between the two groups. We also found a double risk score of developing diabetes in prediabetes patients compared to the control group. No significant differences were found in terms of anthropometric parameters, lipid values, cardiovascular disease and diabetes risk score for the IFG, IGT and IFG + IGT subgroups.* ***Conclusions****: People with prediabetes have features that differentiate them from the general population, both in terms of the history, anthropometric and biochemical characteristics. Increased risk for progression to diabetes, but also highly increased CV risk makes very useful the prevention efforts focused on this population group.*

key words: *prediabetes, IFG, IGT, cardiovascular risk*

Background and Aims

Impaired glucose tolerance (IGT) and impaired fasting glucose (IFG) are defined by 2h post glucose load glycemic values between 140-200 mg/dl, respectively fasting glycemic values between 100-126 mg/dl. Both conditions associate with increased risk for diabetes development and high cardiovascular (CV) risk. Interest in "prediabetes" grew after the publication of clinical studies showing that lifestyle change and pharmacological treatment in these stages can prevent type 2 diabetes (T2DM) [1-5]. Both entities have an increased prevalence, reported between 10% and 30%, depending on age and population groups investigated [6]. The increased CV risk is due both to diabetes per se, and to the very

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frequent association with other risk factors such as hypertension, dyslipidemia and obesity [7]. This risk extends to the population with prediabetes obviously proportional to the modest increases in blood sugar that characterize these stages.

Given the proportions of the diabetes pandemic, prevention measures are urgently needed since "*It is easier to prevent than to cure*". However, preventive actions should target in the first place the known high-risk groups for diabetes. A secondary target is represented by groups of thoroughly investigated subjects (depending on the availability of resources for such investigations) in order to assess periodically the dimensions of an epidemiological phenomenon that becomes more and more alarming.

Research in recent years have enabled us to collect data showing that IFG and IGT have distinct features in terms of pathophysiology so that it is necessary to investigate patients at risk both by fasting glucose and oral glucose tolerance test (OGTT) repeatedly over time in order to undertake preventive measures with maximum effectiveness in preventing T2DM.

Given these premises, the aim of our study was to investigate a population with prediabetes, represented by a group of ambulatory patients, compared to a control group from the general population in respect with the risk for diabetes development and some CV risk parameters.

Materials and Methods

We included some of the patients with suspicion of T2DM that presented at the Diabetes Clinic of the "Nicolae Malaxa" Hospital, generally referred to by general practitioners (GPs) as a result of altered blood sugar found in routine blood test. No prior pre-selection was performed, enrollment of the 124 patients from the study group being at random. The control group consisted of 98 persons employed at a company in Bucharest that made the subject of a previous study in our clinic. Patients signed an inform consent prior to participation in study.

OGTT was performed under standard conditions and the results were interpreted according to WHO criteria for diagnosis of glucose metabolism disorders [8]. Following OGTT, patients with IFG, IGT or both changes were selected. Patients with diabetes were treated according to guidelines in force, and those with normal glucose tolerance test were sent to GPs for follow up.

Patient anamnesis included medical history, focused primarily on metabolic and cardiovascular pathology, and family history mainly related to diabetes. Anthropometric (height, weight waist circumference - WC, BMI) and biochemical (total and HDL cholesterol, triglycerides) parameters were recorded. LDLcholesterol was calculated using Friedewald formula, applicable if triglycerides value were below 450 mg/dl. The presence of CV disease was evaluated.

One of the less expensive methods to investigate the risk of developing diabetes is a risk questionnaire based on epidemiological studies. In our study we chose the FINDRISK questionnaire used previously to estimate diabetes risk by Tuomilehto and his collaborators on the Finnish population [9]. Risk questionnaires are easy, cheap, reproducible, and can reach very high rates of prediction. With the FINDRISK questionnaire, a 85% accuracy in predicting the risk of diabetes in 10 years can be reached.

Statistical analysis included calculation of mean values, standard deviations, minimum values, median values, modal values (for quantitative variables) and proportions or percentages (for qualitative variables).For comparison of mean values, the t Student test was used using the formula: Tc = (mean1-mean2)/standard error of means difference. p-value was calculated in conformity with this value and statistical significance was defined for a $p < 0.05$.

Results

Gender distribution in the group with prediabetes was 46 male patients (37.1%) and 78 female patients (62.9%). Mean age was 56.08 years for the whole group, (between 24 years and 76 years). The best represented was the age group 50-60 years but the age span of the patients was very wide (as shown in Figure 1), demonstrating that prediabetes may occur even in young ages.

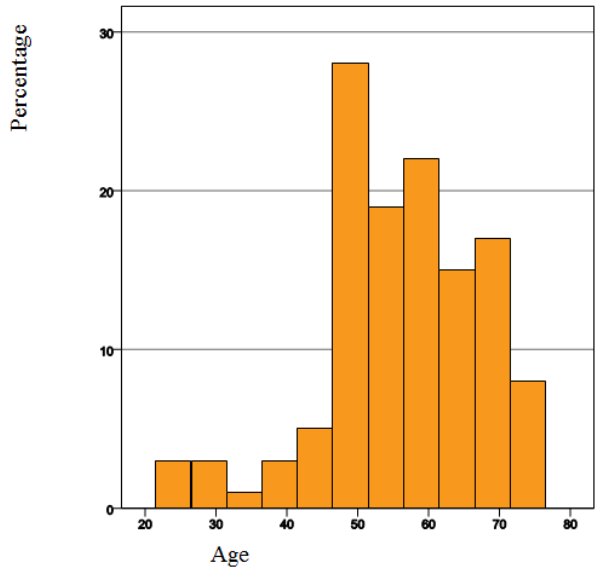

Figure 1. Distribution of patients by age group.

Analysis of BMI showed an average > 30 kg/m², confirming the relationship between obesity and risk of prediabetes. The vast majority of patients were in the category of overweight or obesity as shown in Figure 2. There were also normal weight prediabetes patients, suggesting the involvement of other factors, beyond overweight, in the development of these metabolic disorders.

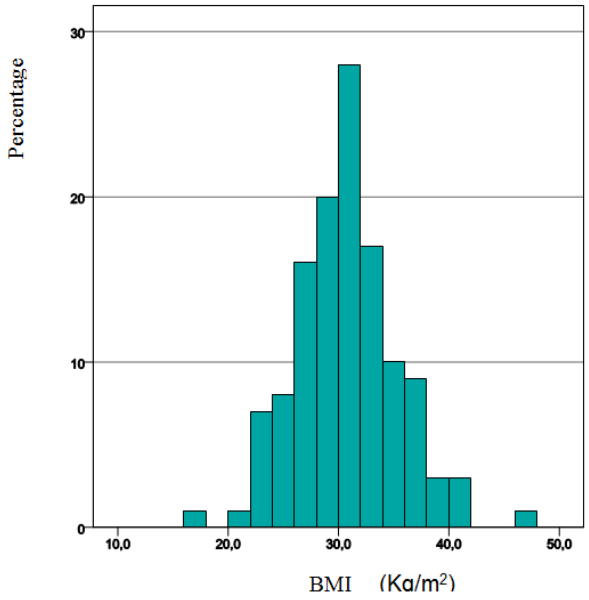

Figure 2. BMI distribution in the study group.

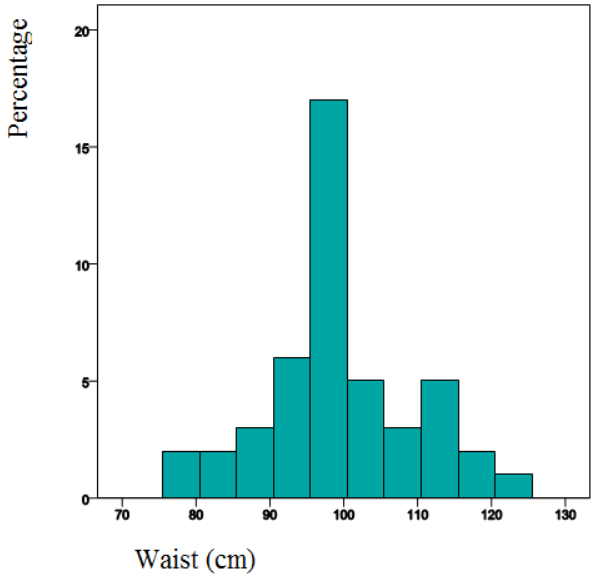

Figure 3. Distribution of waist circumference in prediabetic men.

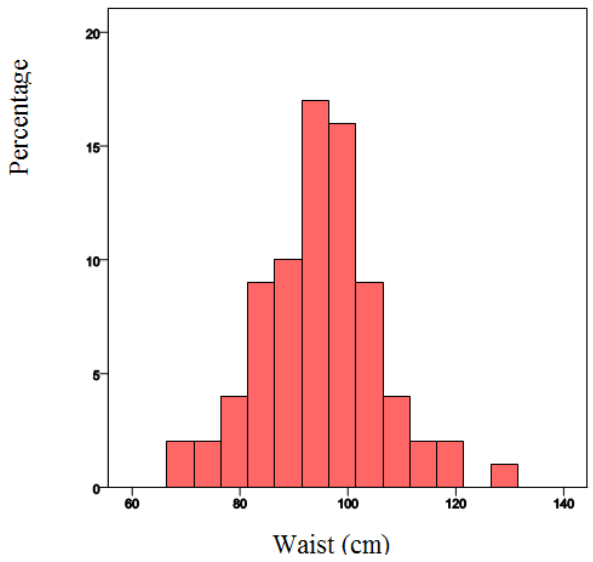

Figure 4. Distribution of waist circumference in women.

For men, the average waist size was > 99cm, which defines abdominal obesity, an important marker for insulin resistance and a major risk factor for prediabetes appearance. The WC data are given in Figure 3.

For women we also confirmed the high prevalence of abdominal obesity (Figure 4), with an average WC of 94.74 cm, well above the accepted limit of 80cm in Caucasians.

Another important factor in the risk of prediabetes is heredity. In our study group, over 30% of patients admitted the existence of diabetes at relatives of 1st and 2nd grade.

Cardiovascular risk and macrovascular damage are the main reasons for the special attention given to prediabetes. Even at this stage, due to early atherosclerosis, CV diseases are frequently present. In our group of prediabetes patients, over one third (34.7%) had proof of macrovascular disease as shown in Figure 5A.

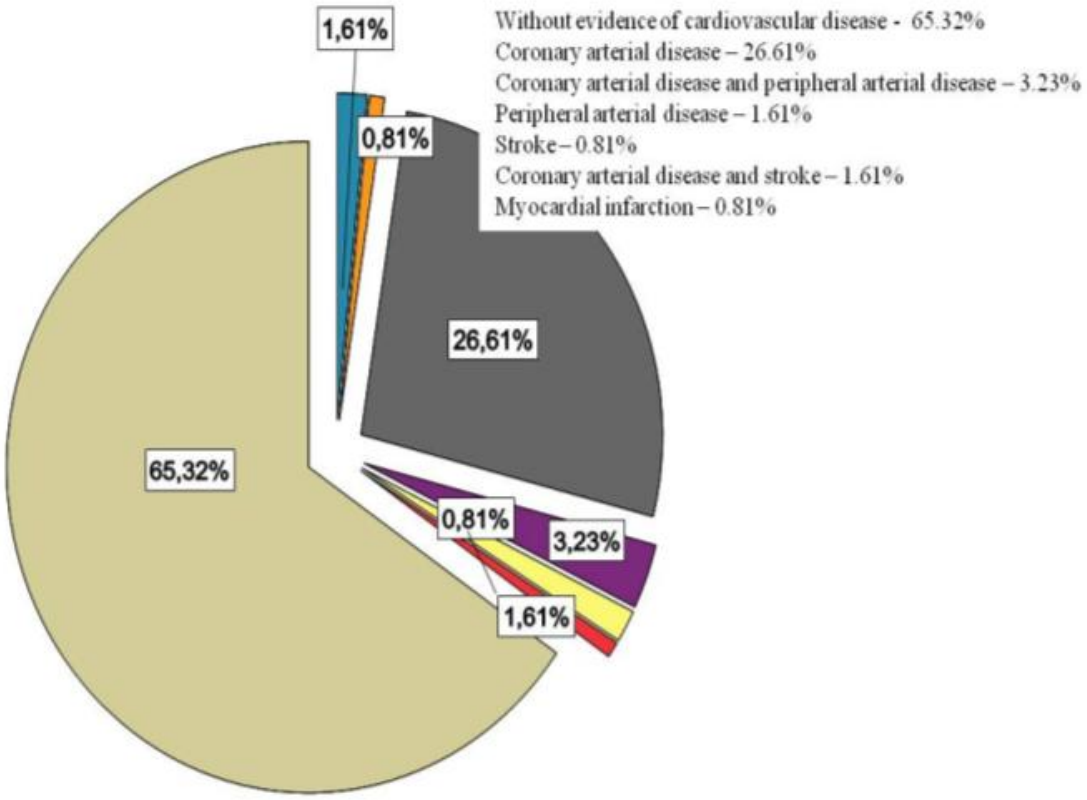

Figure 5A. Distribution of patients according to the presence of CV damage for the entire group studied.

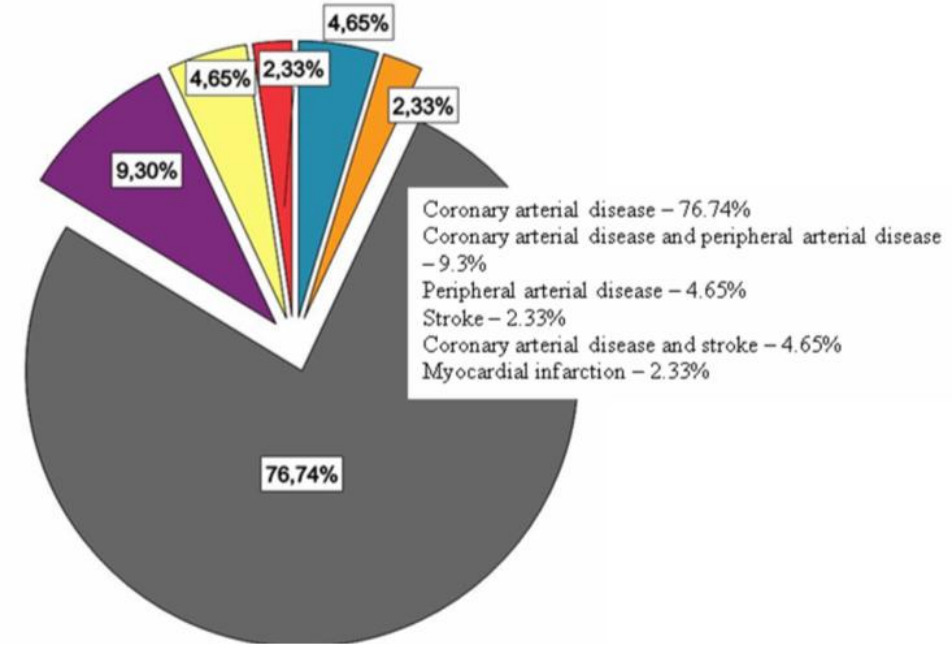

Figure 5B. Distribution of patients according to the presence of CV damage in patients with established cardiovascular disease.

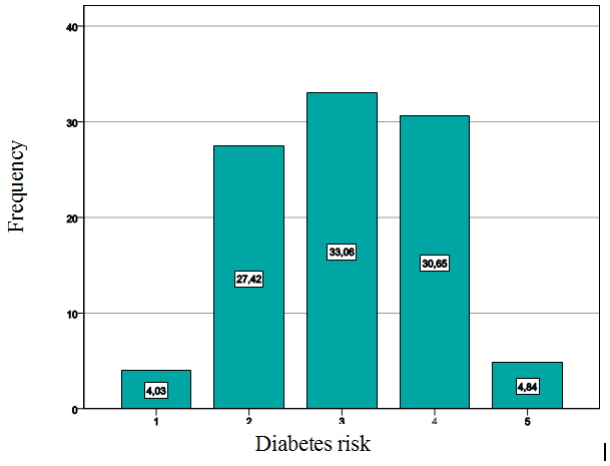

Figure 6. Distribution according to the diabetes risk score.

However we have to mention that the use of more complex diagnostic methods (stress test, echo Doppler imaging, coronarography, etc.) would have probably increased the percentage of those diagnosed with vascular disease. For example, the percentage of those with peripheral artery disease was quite small in our study group (1.61%), being probably under-diagnosed. From the chart that includes only patients with vascular disease (Figure 5B), we notice the high percentage of those with ischemic heart disease, a diagnosis based however solely on history, clinical examination and ECG.

The percentage of subjects with high blood pressure was surprisingly high at nearly 80%. Please notice that not all patients were under treatment, for many of them the diagnosis of hypertension was established at their presentation in our center.

Frequency of dyslipidemia was high in our study group, especially combined dyslipidemia. Mean plasma total cholesterol ~220mg/dl in the prediabetic subjects confirms the high frequency of this CV risk factor in our study group. We should remind that at the beginning of the study statin therapy was not yet widely used. Mean recorded level of triglycerides of approximately 167mg/dl in the prediabetes group was lower than expected, maybe due to the relatively high frequency of treatment with

fibrates. LDLc, the main cardiovascular risk factor, had an average value of 137mg/dl in the prediabetes group, well above the therapeutic target for these patients. Mean HDLc was about 45mg/dl in men and > 52mg/dl in women.

Applying the FINDRISK risk score led, as expected, to the classification of most patients in high diabetes risk categories (Table 2 and Figure 6). Almost 70% were classified into the risk categories 3 to 5.

We also tried to compare the subgroups with IGT, IFG and IGT + IFG but no statistically significant differences were found in terms of anthropometric parameters, lipid profile, cardiovascular disease and diabetes risk score.

Comparing the group with prediabetes and the general population control group, we confirmed the status of increased CV risk category of those with glucose metabolism disorders. From Table 1, we can see that there are statistically significant differences ($p < 0.05$) between average waist, BMI and lipids in the two groups, these parameters being higher in the prediabetes group.

Table 1. Mean Values and Statistical Comparison of the Studied Variables.

Variables	Prediabetes	Control
BMI	30.5 ± 4.89	25.85 ± 4.84
Waist	97.2 ± 11.6	84.59 ± 14.85
Cholesterol	219.19 ± 48.21	199.31 ± 50.35
Triglycerides	166.84 ± 110.94	106.05 ± 87.63
LDL-c	136.8 ± 44.93	130.74 ± 43.37
		p-value < 0.05

Table 2. Risk score for T2DM in the prediabetes and control groups.

Risk categories	Min.	Max	Median	Average	Std. Dev.
IFG	1	5	3	3.24	1.03
IGT	1	5	3	2.93	0.87
IFG+IGT	1	5	3	2.84	1.08
Prediabetes	1	5	3	3.02	1
Control	1	4	1	1.61	0.73

Similar data show that the average risk score for developing T2DM in patients with prediabetes is double the score calculated in the control group.

This correlates with age, weight, BMI, waist, cholesterol, triglycerides, LDLc, which had higher average values in the prediabetes study group as compared to controls from the

general population. A similar correlation was found between the FINDRISK score and cardiovascular disease, family history of diabetes and hypertension (more common in the study group as compared to controls).

Discussion

Comparing the study group with prediabetes and the general population group, we observed a statistically significant difference ($p < 0.05$) for the average BMI (30.50 vs 25.85), indicating that the percentage of overweight and obesity is lower in the general population. It is a real proof of the close relation between the excess weight and the risk of prediabetes, diabetes and metabolic syndrome.

In the group with prediabetes, waist circumference (an indicator of abdominal obesity specific to metabolic syndrome) was above the normal range, both in men (99.22 cm) and in women (94.47 cm). Differences were again statistically significant ($p < 0.05$) between the prediabetes and control groups, people from the general population having a smaller WC (84.59 cm vs. 97.2 cm).

Our data showed highly significant differences ($p < 0.0001$) in terms of frequency of cardiovascular disease, much higher in the group with prediabetes. The result is somewhat different from the literature data (indicating smaller differences), probably explained by the small size of our study groups.

As expected, differences were significant ($p < 0.05$) between the group with prediabetes and the general population group for total cholesterol, triglycerides and LDLc, but not for HDLc.

The analysis of the diabetes risk score evaluated by FINDRISK showed significant differences between the group with prediabetes and the control group, prediabetes patients having a double average risk score (3.02 vs. 1.56).

There were no significant differences between the three categories of glucose metabolism disorders (IFG, IGT and IFG+IGT), probably due to the small size of the study subgroups. This could be an argument for grouping them under the generic term "prediabetes", despite the differences in pathophysiology.

All data presented show that the group with prediabetes is a group with many associated cardiovascular risk factors, comprising anthropometric, biological and historical characteristics. This group of patients is detached from the general population by elements which give the attribute of high-risk group, requiring special monitoring and medical management.

Conclusions

People with prediabetes have specific features that characterize them from the general population, both in terms of the history, the anthropometric and biochemical characteristics. Increased risk of progression to diabetes, but also highly increased cardiovascular risk makes very useful the prevention efforts focused on this population group.

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