

TYPE TWO AND TYPE ONE DIABETES IN THE AGE GROUP 18-40 YEARS

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REZUMAT

Introducere: În prezent este în plină desfășurare la nivel mondial o adevărată epidemie de diabet zaharat (DZ), numărul de cazuri fiind în creștere peste tot în lume, indiferent de vârstă și de categoria socioeconomică. Debutul DZ tip 2 la vârste tinere se însoțește de un risc mai mare de complicații cronice micro și macrovasculare decât dacă boala a debutat la subiecții mai în vârstă. **Obiectiv:** Stabilirea trăsăturilor la debut a și a prevalenței factorilor de risc cardiovasculari la un grup de pacienți cu DZ tip 2 diagnosticat la vârste cuprinse între 18 și 40 de ani și compararea acestora cu un grup de subiecți cu DZ tip 1 de aceeași vârstă, diagnosticați în aceeași perioadă. **Pacienți și metodă:** Au fost înrolați în studiu 283 pacienți cu DZ tip 2 (67.1% bărbați) și 48 pacienți cu DZ tip 1 (60.4% bărbați) cu vârste cuprinse între 18 și 40 de ani, diagnosticați între ianuarie 2006 și decembrie 2008 și înregistrați la Centrul de Diabet Timișoara. Au fost colectate următoarele date din fișele de urmărire ale pacienților: sex, vârsta la diagnostic, tipul DZ, circumstanțe de diagnostic, înălțimea, greutatea maximă și greutatea la diagnostic, glicemia la diagnostic, valorile lipidelor serice, prezența HTA, schema de tratament și complicațiile DZ. Pentru fiecare grup am calculat distribuția în funcție de sex, vârsta medie la debut, IMC-ul mediu, distribuția în funcție de IMC, valorile medii ale lipidelor, prevalența factorilor de risc cardiovascular și a complicațiilor cronice, prevalența sindromului metabolic. Datele au fost prelucrate statistic, pragul de semnificație fiind de 0,05. **Rezultate:** Vârsta pacienților cu DZ tip 1 este semnificativ mai mică față de cea a pacienților cu DZ tip 2 (30,2±17,0 vs. 36,3±3,6 ani, p<0,0001). Majoritatea pacienților cu DZ tip 2 au fost diagnosticați prin măsurarea de rutină a glicemiei à jeun și prin TTGO, în timp ce în DZ tip 1 cea mai frecventă circumstanță de diagnostic a fost cetoza/cetoacidoza diabetică. Obezitatea, dislipidemia și hipertensiunea au fost semnificativ mai frecvente la subiecții cu DZ tip 2. Complicațiile cronice au fost rar întâlnite. Sindromul metabolic a fost prezent la 67,8% din subiecții cu DZ tip 2 și la 10,5% din cei cu DZ tip 1 (p<0,001). **Concluzii:** DZ tip 2 este o afecțiune obișnuită la grupa de vârstă 18-40 de ani, afectează mai ales subiecții obezi și supraponderali și se asociază adesea cu alți factori de risc cardiovasculari, chiar de la diagnostic. Într-o mai mică măsură, acești factori de risc sunt prezenți și la subiecții cu DZ tip 1.

Cuvinte cheie: diabet zaharat tip 2 cu debut precoce, factori de risc cardiovascular, sindrom metabolic, diabet zaharat tip 2

ABSTRACT

Background: A global diabetes epidemic is currently ongoing, with the number of cases increasing worldwide in all age groups and all socio-economic classes. Young adults with early onset T2DM are more likely to develop chronic microvascular and macrovascular complications than older adults with type 2 diabetes. **Aims:** To describe the onset characteristics and to assess the prevalence of cardiovascular risk factors in a group of patients diagnosed with T2DM at ages between 18 and 40 years and to compare them with type 1 DM (T1DM) patients in the same age group and diagnosed in the same period of time. **Patients and methods:** Study groups consisted of 283 T2DM (67.13% males) and 48 T1DM patients (60.4% males) aged between 18 and 40 years, diagnosed between January 2006 and December 2008 at the Diabetes Center Timisoara. Patients data were recorded from the follow-up charts and consisted of gender, age at diagnosis, diabetes type, diagnosis circumstances, height, weight at diagnosis, maximal weight, blood glucose at diagnosis, lipid panel, presence of hypertension, diabetes treatment, presence of chronic diabetes complications, and concomitant diseases. For each group we calculated gender distribution, mean age at onset, distribution depending on the type of onset, average BMI, distribution based on weight status, mean TC, TG and HDLc, prevalence of cardiovascular risk factors, metabolic syndrome (MetS) and of chronic complications. Data was statistically processed with a threshold for significance of 0.05. **Results:** Patients with T1DM were significantly younger compared to those with T2 DM (30.2±17.0 years vs. 36.3±3.6 years, p<0.0001). Most patients from the T2DM group were diagnosed by routine fasting plasma glucose measurement and by OGTT. In T1DM, disease was most commonly diagnosed in the presence of ketosis/ketoacidosis. Obesity, abnormal lipid levels and hypertension were more prevalent in T2DM group. Chronic complications were rarely encountered. MetS was present in 67.8% of T2DM patients vs. 10.5% in T1DM subgroup (p<0.001). **Conclusions:** T2DM is a common disease in the 18-40 years age group. It affects mostly obese and overweight individuals and is very frequently associated with other cardiovascular risk factors, even from the diagnosis. To a lesser extent, cardiovascular risk factors are also present in T1DM.

Key Words: early onset type 2 diabetes, cardiovascular risk factors, metabolic syndrome, type 1 diabetes

INTRODUCTION

Background

We are currently assisting to a global diabetes epidemic, with the number of cases increasing worldwide in all age groups and all socio-economic classes. Global estimates regarding the temporal trends in diabetes mellitus (DM) are worrisome. In 2000, DM affected 171 millions people worldwide, with a general prevalence for all age-groups of 2.8%. It is estimated that in 2030 the prevalence will almost double, to 4.4%,

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with a projected number of diabetic individuals of 366 millions.¹ Most of this increase is attributed to type 2 DM (T2DM). Though the epidemic originally started in the westernized, developed countries, T2DM is no longer a disease of the affluent societies with the greatest estimated increases to be seen in developing countries such as India, China and Arab countries.¹⁻³

T2DM is classically considered to be an adult disease, affecting mostly people aged 40 years or older, however, more and more frequently it is diagnosed in young adults and even in adolescents. The escalating epidemic of T2DM is largely attributable to the fattening of modern society, with a global rise in obesity rates. Obesity and T2DM are called “twin epidemics”, as the latter mirrors and follows the former. Over the last decade of the 20th century obesity has increased by 70% in adults aged 18–29 years, and T2DM has increased in parallel by 70% in adults aged 30–39 years, making young adults the fastest growing adult group for both obesity and T2DM.⁴⁻⁶

Overall diabetes prevalence in Romania, although low, increased constantly since 1990, from 0.65% to 1.6% in 2001, 2.06% in 2004 and to 2.6% in 2007.⁷ According to other authors, the diabetes prevalence in Romania was 4% in 2005.⁸ In Timis county, the number of newly diagnosed T2DM increased from 1,471 in 2000 to 3,296 in 2008.

As the prevalence and severity of chronic complications are directly proportional with diabetes duration, young adults with early onset T2DM are more likely to develop complications such as blindness and kidney failure during their lifetimes, and they have higher rates of diabetes complications and cardiovascular disease (CVD) than older adults with T2DM.⁹⁻¹¹

Aims

The present study aims to characterize clinically, biologically and therapeutically cases with T2DM diagnosed between 2006 and 2008 in age group 18-40 years and to compare them with type 1 DM (T1DM) patients in the same age group and diagnosed in the same interval. Furthermore, it aims to establish the prevalence of cardiovascular risk factors in both diabetes types.

PATIENTS AND METHODS

This is a retrospective study performed at the Diabetes Center Timisoara. Between January 2006 and December 2008 a number of 283 patients diagnosed with T2DM at ages between 18 and 40 years were identified in the database. In the same period 99 patients between 18 and 40 years were diagnosed with

T1DM; 48 of them (for whom the data were available) were included in the study. Patients data were recorded from the follow-up charts and consisted of gender, age at diagnosis, diabetes type, diagnosis circumstances, height, weight at diagnosis, maximal weight, blood glucose at diagnosis, lipid panel (total cholesterol - TC, triglycerides - TG, HDL cholesterol - HDLc), presence of hypertension (known diagnosis or blood-lowering medication), diabetes treatment, presence of chronic diabetes complications, and concomitant diseases. Diabetes type was established based on clinical signs and symptoms, the presence of obesity and the need for insulin treatment. Body mass index (BMI) was computed with the formula $BMI = \text{weight}(\text{kg}) / \text{height}(\text{m})^2$ both for maximal weight and for weight at diagnosis. For each group we calculated gender distribution, mean age at onset, distribution depending on the type of onset, average BMI, distribution based on weight status (normal weight: $BMI > 18 \text{ kg/m}^2$ and $< 25 \text{ kg/m}^2$, overweight: $BMI \geq 25$ and $< 30 \text{ kg/m}^2$, grade I obesity $BMI \geq 30 \text{ kg/m}^2$ and $< 35 \text{ kg/m}^2$, grade II obesity: $BMI \geq 35 \text{ kg/m}^2$ and $< 40 \text{ kg/m}^2$ and grade III or morbid obesity: $BMI \geq 40 \text{ kg/m}^2$), mean TC, TG and HDLc, prevalence of cardiovascular risk factors (abnormal lipids values, hypertension), prevalence of chronic complications, therapeutic regimens. In T2DM group, a supplementary analysis of these parameters was performed for patients divided in two subsets depending on onset modality. Prevalence of metabolic syndrome (MetS) and its components was assessed for each diabetes type. Data were statistically processed using Microsoft Excel (Office 2003) and GraphPad software and differences were assessed using one-way ANOVA and unpaired t test, with a threshold for significance of 0.05.

RESULTS

Patients' characteristics are presented in Table 1. No differences were found regarding gender distribution and background between T2DM and T1DM. Patients with T1DM were significantly younger compared to those with T2DM (30.2 ± 17.0 years vs. 36.3 ± 3.6 years, $p < 0.0001$). In T2DM group, 17 (6%) were between 18 and 30 years, while in T1DM 41.7% were aged between 18 and 30 years.

Data are mean \pm SD unless otherwise indicated; FPG = fasting plasma glucose, Dx = diagnosis, OGTT = oral glucose tolerance test, TC = total cholesterol, TG = triglycerides, HDLc = high density lipoprotein cholesterol, HbA1c = glycated hemoglobin

Almost half of T2DM patients have at least one relative with T2DM, compared to only 30% in T1DM.

Table 1. Characteristics of T2DM and T1DM patients

	T2 DM	T1 DM	p
Total, n	283	48	
Males, n (%)	190 (67,1)	29 (60,4)	ns
Background, urban, n (%)	167 (59.0)	30(62.5)	ns
Age (years)	36.3±3.6	30.2±17.0	< 0.0001
Diagnosis, n (%)			
* routine FPG	184 (65.0)	5 (10.4)	< 0.0001
* OGTT	40 (14.1)	0 (0)	0.0028
* symptoms	54 (19.1)	16 (33.3)	0.0363
* ketosis, ketoacidosis	5 (1.78)	27 (56.3)	< 0.0001
Positive family history for T2DM, n, %	128 (45.2)	14 (29.2)	0.0406
Blood glucose at Dx (mg/dL)	205.9±79.9	353.1±132.8	< 0.0001
BMI at Dx (kg/m ²)	33.3±7.2	23.2±5.0	< 0.0001
Maximal BMI (kg/m ²)	35.8±7.1	27.6±5.9	<0.0001
Obese, n (%)	187 (66.1)	4 (8.3)	< 0.0001
Overweight, n (%)	78 (27.5)	8 (16.7)	ns
Normal weight, n (%)	18 (6.)	36 (75.00)	< 0.0001
Hypertension, n (%)	64 (22.6)	1 (2.1)	< 0.0001
TC (mg/dL) (n)	238.1±78.6 (166)	187.9±43.9 (30)	< 0.0001
TG (mg/dL) (n)	382.9±450.9 (154)	189.5±174.4 (33)	0.0032
HDLc (mg/dL) (n)	43.0±11.9 (101)	47.7±12.9 (19)	ns
% (n) hypercholesterolemia	70.5 (117)	30.00 (9)	< 0.0001
% (n) hypertriglyceridemia	75.3 (116)	39.9 (13)	< 0.0001
% (n) low HDLc	28.7 (29)	21.1 (4)	Ns
Treatment			
Diet, n (%)	79 (27.9)	-	-
Oral medication, n (%)	196 (69.3)	-	-
Insulin, n (%)	8 (2.8)	48 (100%)	< 0.0001
Oral monotherapy, n (%)	135 (47.7)	-	-
Oral association, n (%)	61 (21.5)	-	-
Biguanides, n (%) 177	177 (62.5)	-	-
Secretagogues, n (%)	74 (26.1)	-	-
Mean HbA _{1c} (n)	8.1±2.3 (30)	8.6±2.4 (14)	ns

Most patients from the T2DM group were diagnosed by routine fasting plasma glucose measurement (65.0%) and by oral glucose tolerance test (OGTT) (14.1%). This was possible through the existence of a National Health Program that required mandatory testing of fasting plasma glucose.

In 19.08% of cases, testing for blood glucose was prompted by the presence of suggestive symptoms (polydipsia, polyuria and/or weight loss). Very rarely, patients presented at diagnosis with ketosis or ketoacidosis (1.76%).

Conversely, in T1DM, disease was most commonly diagnosed in the presence of ketosis/ketoacidosis (56.25%). The classical symptoms of diabetes without ketosis/ketoacidosis were present at diagnosis in 33.33%. Weight loss was manifest in both diabetes types and was expressed by a significant decrease in BMI from 35.8 ± 7.1 to 33.3 ± 7.2 kg/m² in T2DM ($p < 0.0001$) and from 27.6 ± 5.9 to 23.2 ± 5.0 kg/m² in T1DM ($p = 0.0002$). BMI decrease was more important in T1DM (4.4 units vs. 2.5 units, respectively), corresponding to the rapid and markedly symptomatic onset characteristic for insulin-dependent diabetes.

Obesity was significantly more prevalent in T2DM group (66.1% vs. 8.3%, $p < 0.0001$), while the percentage of overweight did not differ between groups. Grade III (morbid) obesity (BMI ≥ 40 kg/m²) and grade II obesity (BMI ≥ 35 and < 40 kg/m²) were each present in 14.8% of patients, while grade I obesity (BMI ≥ 30 and < 35 kg/m²) was found in 36.4%. The corresponding percentages for T1DM were: 2.1%, 2.1% and 4.2%, respectively.

More T2DM patients had hypertension compared to T1DM (22.6 % vs. 2.1%, $p < 0.0001$). Lipids measurements were available as follows: TC in 166 T2DM patients and 30 T1DM, TG in 154 T2DM and 33 T1DM, and HDLc in 101 T2DM and 19 T1DM. Mean TC and TG were significantly higher in T2DM patients, while mean HDLc levels were similar. Abnormal TC and TG levels (defined as TC ≥ 200 mg/dL, TG ≥ 150 mg/dL) were significantly more prevalent in T2DM group, while the prevalence of low HDLc (< 39 mg/dL in women, < 35 mg/dL in men) did not differ with the diabetes type.

Glycated hemoglobin (HbA_{1c}) was available for 30 T2DM patients and 14 T1DM patients. Mean HbA_{1c} showed no difference between groups ($8.1 \pm 2.3\%$ vs. $8.6 \pm 2.4\%$, $p = ns$) and reflected a rather poor glycemic control.

As expected, insulin was the sole therapy in T1DM. In T2DM group, most patients (97.2%) were treated either with diet or oral antihyperglycemic drugs. More than one quarter was treated with diet and about 70% received oral medication.

T2DM was stratified depending on the type of onset in two groups: asymptomatic (224 patients), diagnosed by OGTT or by routine fasting plasma glucose, and symptomatic (59 patients), diagnosed based on the presence of symptoms and/or ketoacidosis. Asymptomatic patients were more obese (though not statistically significant) and had significantly lower blood glucose at diagnosis, and TC and TG compared to those who were symptomatic (BMI: 33.7 ± 7.2 vs. 31.7 ± 7.2 kg/m², $p = 0.068$, blood glucose: 188.2 ± 65.4 vs. 275.8 ± 92.0 mg/dL, $p < 0.0001$, TC 228.6 ± 68.2 vs. 263.6 ± 114.2 mg/dL, $p = 0.0012$, TG: 318.2 ± 301.2 vs. 550.0 ± 680.7 mg/dL, $p = 0.0001$). Moreover, in the asymptomatic group, the percentage of patients treated with diet and with monotherapy was higher (32.1 vs. 11.8%, and 47.76 vs. 38.98%, respectively) and that of patients treated with oral antihyperglycemic drugs in association and with insulin was lower (21.0 vs. 49.1%) compared to the symptomatic patients.

Chronic complications were rarely encountered (6.3% in T2DM and 4.2% in T1DM). Nine patients with T2DM had already microvascular complications (one patient had overt diabetic nephropathy, one patient had nephropathy and neuropathy, three had neuropathy and four had retinopathy) and another nine had established cardiovascular disease (two with myocardial infarction and coronary artery bypass, six with angina pectoris, and one with stroke). In the T1DM group, two patients were diagnosed with neuropathy and none had documented retinopathy, nephropathy or cardiovascular disease.

Cardiovascular risk factors are known to associate more closely with T2DM than with T1DM and account for the increased risk for ischemic events in the former.^{12,13} Hypertension, abnormal lipids, obesity and abnormal glucose metabolism, among many others, constitute the core elements of the MetS.¹⁴ In order to assess the prevalence of individual risk factors and that of MetS, we selected all patients in each group in whom a complete lipid panel was available (93 T2DM patients and 19 T1DM patients). The subgroups did not differ significantly from the main groups with respect to sex distribution, mean age at onset, mean BMI and mean glycemia. Furthermore, selected subgroups were similar to the remaining patients for all characteristics, with one exception - patients in T1DM subgroup were significantly younger than those with incomplete measurements. Consequently, we assumed that the selected subgroups are representative samples for each diabetes type. (Table 2)

For each subgroup, we recorded the occurrence of the MetS components and of hypercholesterolemia,

Table 2. Comparison between main groups and subgroups

	T2DM with lipids	T2DM without lipids	T2DM-all	p		T1DM with lipids	T1DM without lipids	T1DM all	p	
	1	2	3	1 vs. 2	1 vs 3	4	5	6	4 vs 5	4 vs 6
total	93	190	283			19	29	48		
M (%)	67.7	66.8	67.1	>0.05	>0.05	57.9	62.0	60.4	>0.05	>0.05
age (years)	36.1 (3.6)	36.5 (3.4)	36.3 (3.6)	>0.05	>0.05	32.8 (6.4)	28.5 (7.0)	30.2 (7.0)	<0.01	>0.05
BMI (kg/m ²)	33.8 (6.4)	33.0 (7.6)	33.3 (7.2)	>0.05	>0.05	22.6 (5.8)	23.6 (4.5)	23.2 (5.0)	>0.05	>0.05
Gly (mg/dL)	211.76 (91.7)	203.83 (73.6)	205.93 (79.9)	>0.05	>0.05	328.9 (113.9)	370.6 (144.7)	353.1 (132.8)	>0.05	>0.05

Data are mean ± SD unless otherwise indicated , M= males, Gly= glycemia, SD= standard deviation

Table 3. WHO clinical criteria for MetS¹⁵

Insulin resistance, identified by one of the following:

- T2DM
- Impaired fasting glucose
- Impaired glucose tolerance, or
- For those with normal fasting glucose levels (<110 mg/dL), glucose uptake below the lowest quartile for background population under investigation under hyperinsulinemic, euglycemic conditions

Plus any two of the following:

- Antihypertensive medication and/or high blood pressure (≥140 mm Hg systolic or ≥90 mm Hg diastolic)
- Plasma triglycerides ≥150 mg/dL (≥1.7 mmol/L and/or HDL cholesterol <35 mg/dL (<0.9 mmol/L) in men or <39 mg/dL (<1.0 mmol/L) in women
- BMI > 30 kg/m² and/or waist:hip ratio > 0.9 in men, > 0.85 in women
- Urinary albumin excretion rate ≥20 µg/min or albumin/creatinine ratio ≥30 mg/g

as well as the prevalence of patients who fulfilled at least 3 criteria for MetS (MetS diagnosis). (Fig. 1) The diagnostic criteria for MetS used were those established by World Health Organization (WHO) in 1999.¹⁵ (Table 3)

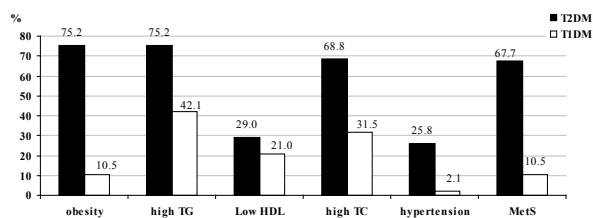


Figure 1. Prevalence of MetS, its individual components and of hypercholesterolemia in T2DM compared to T1DM

All individual components except for low HDLc were significantly more prevalent in T2DM compared to T1DM: obesity 75.2% vs. 10.5% (p<0.001), high TG 75.2% vs. 42.1% (p=0.0065), high TC 68.8% vs. 31.5%, hypertension 25.8% vs. 2.1% (p<0.0001). Low

HDLc was similarly prevalent in the two subgroups. MetS (three or more criteria present) was present in 67.77% of T2DM patients vs. 10.52% in T1DM subgroup (p<0.001). Two elements of MetS (DM + one from the other criteria) were found in 25.80% of T2DM and 47.36% of T1 DM patients (p= ns).

DISCUSSIONS

T2DM usually has an insidious onset, with a long evolution prior to becoming clinically manifest, ranging in many cases from 5 to 10 years.¹⁶ Outside screening programs, it is most commonly diagnosed when the patient develops suggestive symptoms such as excessive thirst, polyuria, weight loss, hunger. As hyperglycemia develops gradually, frequently the patient is asymptomatic, but this degree of hyperglycemia is sufficient to cause pathological changes in target tissues. Many of these asymptomatic patients are at increased risk to develop chronic diabetes complications.^{9,10,17,18} Epidemiological data

show that retinopathy starts to develop at least 7 years before the clinical diagnosis of T2DM. The patients with T2DM are at increased risk for cardiovascular disease (CVD) (coronary heart disease, stroke and peripheral artery disease) compared to non-diabetic individuals, also because they are more likely to have abnormal lipid levels, hypertension and obesity.¹⁹⁻²²

The development of chronic complications may be prevented both by an active screening for T2DM and impaired glucose tolerance in at-risk individuals and by an intensive management once the disease has developed. The current screening recommendations are presented in Table 4.²²

The T2DM patients in this study who were diagnosed in the asymptomatic phase using fasting plasma glucose or OGTT had milder metabolic derangements and a lower fasting plasma glucose that was managed easier with less medication.

In 2005, IDF published a new, revised definition for MetS that essentially contains the same criteria but in a different order, requesting as mandatory element central obesity (expressed by an increased waist circumference).¹⁴ When the various sets of criteria were compared in the same population, the IDF definition elicited a higher prevalence of MetS compared to the WHO, NCEP-ATP III and AACE definitions.^{31,32} In the present analysis, we could not use the IDF criteria as waist circumference was available only for a few patients. Although the WHO definition was better suited for the data available, we could not fully explore the prevalence for all the components (e.g., urinary albumin excretion) and the missing waist to hip ratio may have led to smaller prevalence of obesity, therefore our results probably underestimate the true prevalence of MetS in the studied patients.

Table 4. Criteria for testing for pre-diabetes and diabetes in asymptomatic adult individuals²²

Testing should be considered in all adults who are overweight (BMI ≥ 25 kg/m²) and have additional risk factors:

- physical inactivity
- first-degree relative with diabetes
- members of a high-risk ethnic population (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
- women who delivered a baby weighing >9 lb (>4 kg) or were diagnosed with GDM
- hypertension ($\geq 140/90$ mmHg or on therapy for hypertension)
- HDL cholesterol level <35 mg/dl (0.90 mmol/l) and/or a triglyceride level >250 mg/dl (2.82 mmol/l)
- women with polycystic ovarian syndrome (PCOS)
- IGT or IFG on previous testing
- other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)
- history of CVD

In the absence of the above criteria, testing for pre-diabetes and diabetes should begin at age 45 years

If results are normal, testing should be repeated at least at 3-year intervals, with consideration of more frequent testing depending on initial results and risk status

Both fasting plasma glucose and OGTT are accepted as screening methods.

GDM= gestational diabetes mellitus, IGT= impaired glucose tolerance, IFG= impaired fasting glucose, CVD= cardiovascular disease

Subjects with T2DM are at increased risk for cardiovascular disorders and often exhibit various cardiovascular risk factors such as abnormal lipid levels, hypertension and obesity.^{23,24} The clustering of these risk factors, with insulin resistance as a common denominator, has been called the metabolic syndrome (MetS) and has been associated with progressing atherosclerosis and higher risk for cardiovascular events.²⁵⁻²⁸ Currently there are four definitions: the criteria of the World Health Organization (WHO) consultation group, the criteria of the National Cholesterol Education Program (NCEP) Expert Panel, the criteria of the American Association of Clinical Endocrinologists (AACE), and the International Diabetes Federation (IDF) Criteria.^{15,29,30}

Cardiovascular risk factors are also present, albeit less frequently, in T1DM patients and are associated with the progression of chronic complications such as nephropathy and retinopathy.^{12,33-35}

Several studies have been published regarding the prevalence of cardiovascular risk factors in young adults with T2DM and T1DM. Compared to our study, FinRisk Study found much higher prevalence for MetS in T2DM patients (91.5% in men and 82.7% in women) as well as for obesity (93.1% in men and 81.6% in women) and hypertension (78.1% in men and 76.4% in women), but similar for dyslipidemia (76.9% in men and 69.4% in women).²¹ These differences are explained by the impossibility to apply all diagnostic criteria for MetS in our patients but also by the fact

the patients in FinRisk Study were older (between 40 and 65 years). West NA et al have found a prevalence of 27% for hypertension, 86% for obesity, 27% for high triglycerides, 25% for low HDLc in young (10-22 years) T2DM patients at diagnosis.³⁶ In another USA study that included T2DM and T1DM patients aged between 18 and 44 years, the prevalence of obesity was 87.3% in T2DM and 38.5% in T1DM, dyslipidemia was present in 60.2% of T2DM and in 40.9% of T1DM, while hypertension was found in 24.1% of type 1 and 47.8% of type 2 patients. Three or more cardiovascular risk factors were found in 78.3% of type 2 and 32.8% of type 1 patients.³⁷ Finally, in a group of 277 early-onset (less than 45 years old) T2DM patients, 49% had hypertension (vs. 61% in older onset), 82% had abnormal lipid levels (vs. 78% in older onset) and had a mean BMI of 39 kg/m² (vs. 33 kg/m² in older onset).⁶

The prevalence of dyslipidemia (defined as LDLc \geq 130 mg/dl, HDLc $<$ 40 mg/dl, total TC \geq 200 mg/dl, or TG \geq 150 mg/dl) in T1DM patients aged between 20 and 50 years was 47% in a study conducted in Denver, USA.³⁸ In Germany, in a group of over 27,000 T1DM patients of all ages more than half of the patients in the adult group had at least one cardiovascular risk factor, ~32% of the patients had any dyslipidemia, ~30% had high cholesterol levels, ~11% of the patients had hypertension, and obesity was present in approximately 8%.³³ Overall prevalence of MetS was 33% in age group 18-30 years and 40% in age group 30-40 years in a study conducted on 2,415 T1DM patients in Finland.¹²

In the present study, microvascular and macrovascular complications were present in a small proportion of patients with T2DM. Given the short diabetes duration, the presence of microvascular complications in T2DM patients suggests a prolonged subclinical evolution prior to diagnosis. Several papers have shown that early onset T2DM is associated with an increased risk for microvascular complications such as retinopathy and nephropathy.³⁹⁻⁴¹

Although CVD was present in only 3.15% of T2DM, it is worrying for a couple of reasons. Firstly, this was not a prevalence study for CVD and the data were provided by follow-up charts that record concomitant diseases as reported by patients or from hospital discharge notes. Thus, no attempt was made to actively diagnose CVD and the resulting prevalence is only a conservative estimate. Secondly, among the nine cases, two had myocardial infarction and coronary artery bypass and one had a stroke, suggesting an accelerated atherosclerosis process. The risk of macrovascular complications in T2DM

patients with early onset was demonstrated in study performed in USA on 7,800 T2DM patients. Patients with DM onset at ages between 18 and 44 years had an 8-fold increase in the overall risk for cardiovascular events (myocardial infarction, cerebrovascular disease, coronary artery bypass and percutaneous coronary angioplasty, peripheral artery disease) compared to non-diabetic age-matched subjects. The risk for myocardial infarction increased 14-fold and that for stroke 30-fold compared to non-diabetic controls. For comparison, the overall risk was 4-fold increased in older-onset ($>$ 45 years) T2DM patients.⁴²

CONCLUSIONS

T2DM is a common disease in the 18-40 years age group. It affects mostly obese and overweight individuals and is associated with other cardiovascular risk factors such as dyslipidemia and hypertension, even from diagnosis. Although a very conservative estimate, the prevalence of MetS in these individuals is very high (67.74%), close to the data reported in older diabetic adults. This cluster of risk factors favors accelerated atherogenesis leading to development of severe CVD in a short period of time. Consequently, early-onset T2DM patients face potentially devastating diseases while at an active age.^{43,44}

Active screening in individuals at risk and aggressive management of DM as well as of the other comorbidities are the only available weapons for prevention of this bleak outcome. The role of the early diagnosis is supported by the finding of milder hyperglycemia and metabolic anomalies in T2DM patients who were diagnosed in the asymptomatic phase using fasting plasma glucose or OGTT.

To a lesser extent, cardiovascular risk factors are also present in T1DM and should be systematically sought and treated.

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