



# ASSESSMENT OF METABOLIC SYNDROME COMPONENTS IN NEWLY DIAGNOSED TYPE 2 DIABETES

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## Abstract

Metabolic syndrome (MS) consists of multiple cardiometabolic risk factors that tend to aggregate in an individual more often than only by chance. It frequently coexists with type 2 diabetes mellitus (T2DM). The aim of the present study is to characterize the prevalence of MS and its traits, as well as the modalities of clustering of the components, in 1111 (49.6% female, 50.4% male; mean age of 59 years) newly diagnosed T2DM patients from an outpatient diabetes clinic. According to the International Diabetes Federation (IDF)'s definition, the abdominal obesity is one of "any three of five characteristics" in a person with MS. As all our patients were diabetics, in order to be defined as having MS they must have had a waist circumference  $\geq 94$  cm for men and  $\geq 80$  cm for women and at least one of any of the following factors: elevated triglycerides:  $\geq 150$  mg/dL or specific treatment for this lipid abnormality; decreased HDL-cholesterol:  $< 40$  mg/dL in men;  $< 50$  mg/dL in women, or specific treatment for this lipid abnormality; high blood pressure: systolic blood pressure  $\geq 130$  and/or diastolic blood pressure  $\geq 85$  mm Hg, or antihypertensive drug treatment. In the latest published consensus definition the visceral obesity is no longer an obligatory component for MS diagnosis, three or more of the following criteria must be met: (i) abdominal obesity: increased waist circumference, (ii) elevated triglycerides:  $\geq 150$  mg/dL, (iii) decreased HDL-cholesterol:  $< 40$  mg/dL in men,  $< 50$  mg/dL in women, (iv) increased blood pressure systolic  $\geq 130$  and/or diastolic  $\geq 85$  mm Hg, and (v) increased fasting glucose  $> 100$  mg/dL. Metabolic syndrome incidence was high, no matter what definition was used: 89.7% (IDF's definition), 92.3% (the 2009 harmonized definition with a cut-off value for waist of 80 cm in women and 94 cm in men) and 88.6% (the 2009 harmonized definition with a cut-off value for waist of 88 cm in women and 102 cm in men). The concordance between the three definitions was 85.3% (higher in women). Most of the patients with MS fulfilled four of the criteria. Beside hyperglycemia, the decreasing frequency of MS traits was: increased waist circumference (96.4%), high blood pressure (84.8%), low HDL cholesterol (63.9%) and high triglycerides (57.9%). Among patients with MS, the increased waist and low HDL cholesterol were more frequent findings in women than in men, while hypertriglyceridemia was more frequent in men. Mean value for both systolic and diastolic pressure were higher in women. In sum, the results underline the high prevalence of MS among subjects with newly diagnosed T2DM and in majority of cases, four components are clustering. The clustering appears to be dependent on excess of visceral adipose tissue and has a different pattern depending on gender.

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## Introduction

Metabolic syndrome (MS) consists in multiple cardiometabolic risk factors that tend to aggregate more often than only by chance. It frequently coexists with type 2 diabetes, and in this combination, the risk is increased even more (1). The MS components include elevated glycemia (type 2 diabetes included), atherogenic dyslipidemia, elevated blood pressure, a prothrombotic and a proinflammatory state (2, 3). The MS is commonly affecting about 25-30% of the general population in Europe (4-9) and the prevalence is increasing. The prevalence is even higher in people with type 2 diabetes, varying between 70 and 91.5% depending on which definition was used or the type of population studied (10-14).

The aim of the present study is to determine the prevalence of MS and to characterize its traits in an adult population of newly diagnosed type 2 diabetic patients. Another objective was to describe the modalities of clustering the components of the metabolic syndrome in this population and to examine if there are differences between genders. As the prevalence varies with different definitions, we used the 2005 International Diabetes Federation (IDF) criteria (3) and the consensus definition of the IDF and the American Heart Association, National Heart, Lung, and Blood Institute, World Heart Federation, International Atherosclerosis Society and International Association for the Study of Obesity (15).

## Subjects and methods

### Subjects

We included in our study 1111 subjects with newly discovered type 2 diabetes from an outpatient diabetes clinic. The subjects, aged 30-89 years, with a similar gender distribution (551-49.6% female, 560-50.4% male) were entered into a descriptive, cross-sectional analysis with the aim to characterize the prevalence of MS and its traits. The subjects were referred to the diabetes clinic by their general practitioners, by other specialists or by self-referral. Initially we entered all consecutive patients that were registered at the clinic with newly diagnosed type 2 diabetes, during 18 months, but we kept for the analysis only the subjects with complete clinical, anthropometric, and biochemical data.

### Methods

The subject's data were recorded during the visit at the clinic. The data about lifestyle, family history, personal medical history, and concomitant medication were noted. The physical examination included weight (in light clothing), height (barefoot), waist circumference (measured with the subject standing, at mid distance between the lowest rib and the iliac crest, at the end of normal expiration), and blood pressure measurements. The

body mass index (BMI) was calculated as weight (kg)/ height (m<sup>2</sup>). Fasting venous blood samples were taken to determine serum glucose, total cholesterol, triglycerides (TG), high density cholesterol (HDL-cholesterol), creatinine, transaminases (AST, ALT), and glycated hemoglobin (HbA1c). Low density cholesterol (LDL-cholesterol) was calculated using Friedewald formula. The samples were analyzed at the center's laboratory. The history of cerebrovascular disease was of particular interest (documented coronary heart disease, previous myocardial infarction, stroke, peripheral arterial disease).

According to the IDF definition (3), the central (abdominal) obesity is mandatory for diagnosis of the MS. As all our patients were diabetics, in order to be defined as having MS they must have had a waist circumference  $\geq 94$  cm for men and  $\geq 80$  cm for women and any at least one another factor of the following factors: elevated triglycerides:  $\geq 150$  mg/dL or specific treatment for this lipid abnormality; decreased HDL-cholesterol:  $< 40$  mg/dL in men;  $< 50$  mg/dL in women, or specific treatment for this lipid abnormality; high blood pressure: systolic blood pressure  $\geq 130$  and/or diastolic blood pressure  $\geq 85$  mm Hg, or antihypertensive drug treatment.

In the latest published consensus definition (15) the central obesity is no longer an obligatory component. In order to establish MS diagnosis, three or more of the following criteria must be met: (i) abdominal obesity: increased waist circumference, (ii) elevated triglycerides:  $\geq 150$  mg/dL or specific treatment for this lipid abnormality, (iii) decreased HDL-cholesterol:  $< 40$  mg/dL in men,  $< 50$  mg/dL in women, or specific treatment for this lipid abnormality, (iv) increased blood pressure systolic  $\geq 130$  and/or diastolic  $\geq 85$  mm Hg, or antihypertensive drug treatment in patient with history of hypertension, and (v) increased fasting glucose  $> 100$  mg/dL, or drug treatment of increased glucose. All of our patients had diabetes so they had one component of the syndrome. For waist circumference in Europeans it is recommended that either the IDF or AHA/NHLBI cut points to be used. At waist circumference of  $\geq 94$  cm for men and  $\geq 80$  cm for women (IDF cut points), the risk is increased (consensus definition I); but the risk is substantially greater when the waist circumference is  $\geq 102$  cm for men and  $\geq 88$  cm for women (AHA/NHLBI cut points). We tested both sets of cut points in our study population. The drugs used for increased triglycerides and reduced HDL cholesterol were fibrates. We considered those using high-dose of  $\omega$ -3 fatty acids as having high triglycerides.

### Statistical analysis

The statistical analysis was performed with Epi Info 7.1.0.6 statistical software (Centre for Disease Control, Atlanta). First we realized a descriptive analysis of the variables. The population

clinical and biochemical characteristics were presented as mean  $\pm$  standard deviation. Variables values were compared between women and men, and between those with or without the metabolic syndrome. A p value of  $<0.05$  was considered to indicate a significant difference. We also identified a metabolic syndrome component association.

## Results

The clinical and metabolic characteristics of patients are presented in Table 1. The mean age was 59 years, women being slightly older ( $p<0.05$ ) than men. Women had higher BMI and waist circumference than the women. For the metabolic characteristics, men had significantly higher values for serum triglycerides and transaminases ( $p<0.05$ ).

Metabolic syndrome prevalence was high no matter what definition was used, but there were different prevalence rates according to the different definitions. Respectively, the prevalence was: 89.7% (IDF definition), 92.3% (the harmonized definition with a cut off value for waist of 80 cm in women and 94 cm in men) and 88.6% (the harmonized definition with a cut off value for waist of 88 cm in women and 102 cm in men). The

harmonized definition with a cut off value for waist of 80 cm in women and 94 cm in men indicates greater prevalence than other definitions.

Taking into consideration the number of the criteria fulfilled for MS definition, it was noticed that no matter what definition was used most of the patients identified with metabolic syndrome have fulfilled four criteria. In the IDF's definition, on the second position as frequency are placed the patients that fulfilled five criteria. In the harmonized definition, on the second position as frequency are placed the patients that fulfilled three criteria. After diabetes, which was present in all patients, the next most frequent MS trait was increased waist circumference, being present in 94,2% of subjects if the IDF cut points were used, or in 80,9% of subjects if the AHA/NHLBI cut points were used. The highest proportion of subjects with waist trait present and identified as having metabolic syndrome was noticed for the harmonized definition with a cut off value for waist of 88 cm in women and 102 cm in men (96.4%).

The concordance between the three definitions was 85.3%. Agreement between different definitions was higher for women than for men, as described also in other diabetic populations

**Table 1.** Clinical and metabolic characteristics of patients

Gender	Females			Males			P	Total		
	N	Mean	St.dev.	N	Mean	St.dev.		N	Mean	St.dev.
Age* (years)	551	59,79	10,188	560	57,97	10,945	0,004	1111	58,87	10,611
BMI* (kg/m <sup>2</sup> )		32,711	6,1451		30,475	5,1898	0,000		31,584	5,7901
Waist* (cm)		105,17	12,998		107,94	12,124	0,000		106,57	12,635
Total cholest (mg/dL)		218,92	54,28		216,09	58,15	NS		217,49	56,259
HDL-cholesterol* (mg/dL)		46,14	13,08		40,72	11,24	0,000		43,41	12,488
LDL-cholesterol (mg/dL)		138,22	48,586		134,68	44,126	NS		136,49	46,468
Non HDL-cholesterol (mg/dL)		172,77	54,075		175,37	57,910	NS		174,09	56,031
TG* (mg/dL)		180,85	149,81		212,18	188,79	0,000		196,65	171,21
AST* (UI/L)		25,21	14,022		27,38	15,325	0,014		26,31	14,726
ALT* (UI/L)		29,60	17,97		34,18	19,69	0,000		31,91	18,99
AST/ALT*		0,938	0,349		0,893	0,407	0,049		0,916	0,379
Serum Creatinine* (mg/dL)		0,74	0,200		0,92	0,201	0,000		0,83	0,218

(14). The consensus (harmonized) definition with a cut-off value for waist of 88 cm in women and 102 cm in men tended to identify more associated metabolic disturbances, although not reaching statistical significance. For this reason and for the fact that all MS traits appeared with higher frequency than in the other two compared definitions ( $p < 0.05$ ) we further analyzed the data referring only to this definition.

In our study population, women with MS were more numerous than men (52.4% vs. 47.6%,  $p < 0.05$ ). Different published papers reported different gender distribution of the metabolic syndrome.

In literature, it was described an increasing prevalence of MS with increasing age (17, 18). The age distribution of patients with MS is presented in Figure 1. According to this distribution it can be concluded that 4 out of 10 patients with MS are placed in the group 50-59 years and 3 out of 10 patients in the group 60-69 years.

Most of the patients with MS fulfilled four of the criteria. Beside hyperglycemia, the decreasing frequency of metabolic syndrome traits was: increased waist circumference (96.4%), high blood pressure (84.8%), low HDL cholesterol (63.9%) and high triglycerides (57.9%). The frequency of the individual MS criteria fulfilled had significant difference between genders for:

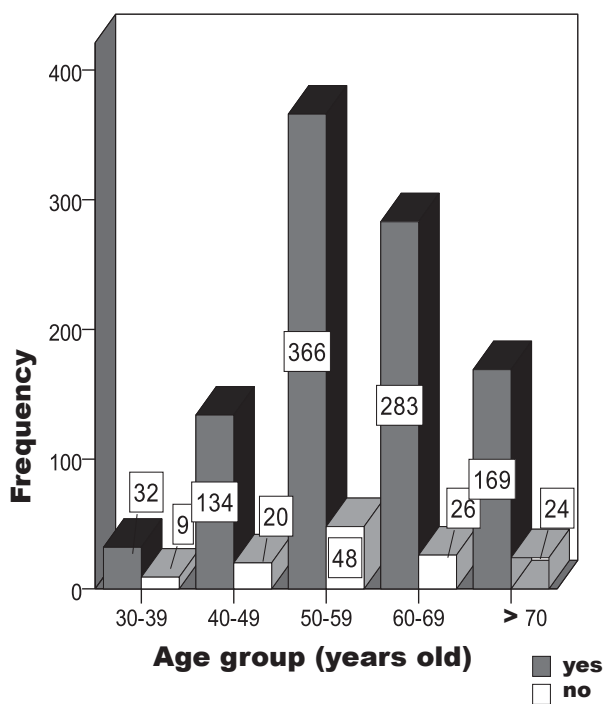
large waist circumference, low HDL cholesterol - more frequent in women, elevated triglycerides - more frequent in men. The frequencies of different MS traits are presented in table 2. Mean value for both systolic and diastolic pressure were higher in women ( $p < 0.05$ ).

The component association was different depending on gender. In women the following ranking of components associations was observed: 34.1% associated increased waist, high blood pressure, increase triglycerides, low HDL cholesterol, 23.1% associated increased waist, high blood pressure, low HDL cholesterol, and 19.6% associated only increased waist and high blood pressure. The profile is significantly different for men, where the ranking of components associations is: 27.1% associated increased waist, high blood pressure, increase triglycerides, low HDL cholesterol, 18.6% associated increased waist and high blood pressure, and 13.7% associated increased waist, high blood pressure, low HDL cholesterol.

## Discussion

The concept of MS is nowadays identifying centrally obese people with increased risk for cardiovascular disease and, if not already present, type 2 diabetes. Although there are different definitions in use, and the prevalence of the MS varies with the definition used, it is no doubt that its prevalence is high and increasing all over the world. In special populations like patients with type 2 diabetes, the reported prevalence is even higher (10-14), the syndrome being closely associated with type 2 diabetes. In our study, the prevalence was: 89.7% (IDF's definition), 92.3% (the harmonized definition with a cut off value for waist of 80 cm in women and 94 cm in men) and 88.6% (the harmonized definition with a cut off value for waist of 88 cm in women and 102 cm in men). The prevalence was higher in women than in men (52.4% vs. 47.6%,  $p < 0.05$ ). Other published papers reported different gender distribution of MS. Some of the studies in European subjects reported higher prevalence in women, similar to our findings (14, 16), while others reported higher prevalence in men (11). The highest prevalence was noticed for subjects aged 50-59 years, followed by subjects aged 60-69 years, and by the subjects older than 70 years.

The MS traits clustered in studied patients, most of them fulfilling four criteria. After diabetes, the most common MS trait was large waist circumference, underlining the importance of central obesity in these patients. We further analyzed gender differences in our patients. Among those with metabolic syndrome, the increased waist and low HDL cholesterol were more frequent findings in women than in men ( $p < 0.05$ ), while hypertriglyceridemia was more frequent in men ( $p < 0.05$ ). The component association was also different depending on gender.



**Figure 1.** Age distribution of patients with metabolic syndrome.

**Table 2.** Frequencies of different metabolic syndrome traits in subjects with type 2 diabetes

Subjects	Metabolic syndrome traits			
	Large waist circumference*	High blood pressure <sup>§</sup>	Low HDL cholesterol*	Elevated triglycerides <sup>#</sup>
<b>Women fulfilling the criteria</b> N (% of total subjects fulfilling the criteria)	492 (56.7%)	446 (53.4%)	357 (56.8%)	275 (48.2%)
% within all women	95.3%	86.4%	69.2%	53.3%
<b>Men fulfilling the criteria</b> N (% of total subjects fulfilling the criteria)	375 (43.3%)	375 (43.3%)	272 (43.2%)	295 (51.8%)
% within all men	80.1%	83.1%	58.1%	63.0%
<b>Total subjects fulfilling the criteria N</b>	867	835	629	570

p=0.000; # p=0.001; § p=0.087, NS.

We identified a different pattern of the components clustering in females *versus* males.

## Conclusion

The results underline the high prevalence of MS among subjects with newly diagnosed type 2 diabetes and the fact that in majority of cases, four components are clustering. The clustering appears to be dependent on visceral adiposity and has a different pattern depending on gender. The identification of traits of MS at the time of diagnosis of type 2 diabetes might be a useful tool for identifying subjects having an increased (global) cardio-metabolic risk. A high disease burden is increased taking into account that MS is often associated with other disorders such as advanced atherosclerosis, nonalcoholic fatty liver disease or polycystic ovary syndrome. The recognition of MS in patients with type 2 diabetes from the time of its diagnosis is an important “preventive” measure in an integrated approach aimed at the reduction of associated comorbidities and disease costs.

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