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EPIDEMIOLOGICAL CHARACTERISTICS OF METABOLIC SYNDROME IN THE POPULATION OF HUNEDOARA COUNTY

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Abstract

The metabolic syndrome (MS) is an association of proatherogenic clinical and biochemical abnormalities, that is considered to contribute to the epidemic of diabetes mellitus and cardiovascular diseases. In this study, we aimed to evaluate the prevalence of MS in the general population of Hunedoara County and to identify its components and factors that influence its presence. A cross-sectional study was conducted, which included 4677 subjects. Applying the International Diabetes Federation 2005 definition we found that 2141 people had MS, giving a prevalence of 45.78%.

keywords: *Metabolic syndrome, type 2 diabetes mellitus, glucose tolerance*

Introduction

The metabolic syndrome (MS) is an association of proatherogenic clinical and biochemical abnormalities, that is considered to contribute to the epidemic of diabetes mellitus (DM) and cardiovascular diseases (CVD). The prevalence is growing, together with the increasing rate of obesity. The relative risk for DM of persons with MS is 3.4-5.2, while the relative risk for cardiovascular events is 1.5-2.0 [1, 2, 3].

In this study, we aimed to evaluate the prevalence of MS in the general population of Hunedoara County and to identify its components and factors that influence its presence.

Material and Method

The study was designed as a cross-sectional investigation and was based on the General Practitioners (GPs) lists of people. We randomly selected 4677 subjects, from all over the county, both from urban and rural

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areas, all Caucasians, aged between 20-90 years. Demographical data, anthropometric measurements and a minimum of biochemical parameters were collected. The subjects were instructed to fast minimum 8 hours overnight before examination. All cases were analyzed at *Bioclinica Laboratory Deva* on Architect analyzer. Glycemia was determined using hexokinase method, for total cholesterol the enzymatic method was used, for triglycerides, glycerolphosphate oxidase method, for LDLc, liquid selective detergent homogenous method and for HDLc, accelerator selective detergent homogenous metod. 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. Body mass index (BMI) was calculated as weight [kg] divided by the square of height [m]. The ratio between waist circumference and height was also calculated (the results were multiplied by 100).

We used the International Diabetes Federation (IDF) criteria from 2005 to define the MS (table 1) [1].

Table 1. International Diabetes Federation definition for metabolic syndrome (2005)

Central obesity: waist circumference ≥ 94 cm for men and ≥ 80 for women + any two of the following: Triglycerides ≥150mg/dl or specific treatment for this abnormality HDLc <40mg/dl for men and <50mg/dl for women or specific treatment for this abnormality Arterial hypertension (HA): 130/85mmHg or medication Fasting plasma glucose ≥100mg/dl or previously diagnosed DM

In each group of glucose tolerance, we separately analyzed the subgroups with and without MS.

Statistical analysis was performed using the statistical package SPSS v.15.0. For describing the numerical variables we used the mean and standard deviation, while for the categorical ones we used the absolute and relative frequencies. For the statistical tests, the 0.05 (i.e. 5%) two-tailed level of significance was considered. We applied ANOVA tests for comparing numerical parameters from more than two groups and the Bonferonni post-hoc testing for multiple comparisons. In the case of categorical variables, for assessing the statistical significance of their potential association, we employed the Pearson Chi-square testing procedure.

Results

From the 4677 subjects analyzed, 1088 were diagnosed with DM, having the fasting glycemia ≥126mg/dl or already known DM. According to the World Health Organisation (WHO) criteria, we found 443 persons who had impaired fasting glycemia (IFG) (fasting glycemia 110mg/dl – 125mg/dl) [4, 5]. Using the American Diabetes Association (ADA) criteria, 1228 people had IFG (fasting glycemia 100mg/dl – 125mg/dl) [7, 8, 9]. We divided the subjects in three groups: DM, IFG and normal glucose tolerance (NGT), separately for both WHO and ADA criteria of

glucose tolerance. Applying the IDF 2005 definition we found that 2141 people had MS, giving a prevalence of 45.78%.

The glucose tolerance categories based on WHO criteria.

The main characteristics of the study subjects, according to WHO criteria for glucose tolerance, are presented in Table 2a. In the sub-group with DM, 773 subjects had MS, giving a prevalence of 71.05%. In the sub-group with IFG, 310 persons (69.98%) had MS, while at the people with NGT, MS was present in 33.63% of cases. We then considered the subjects with MS as a sub-group of higher risk in all these three categories and applied the analysis of variance (ANOVA) to see whether there are any differences for the anthropometric measurements and biochemical parameters. We have observed that, the differences between groups were extremely significant, excepting the triglycerides. Furthermore, as a post-hoc test, we applied the Bonferonni testing procedure for finding the pairs for which a statistically significant difference exists (Table 2b).

Table 2a. The main characteristics of the study subjects, according to WHO criteria for glucose tolerance.

Total 4677 subjects	DM N=1088 (23.26%)		IFG (WHO) N=443 (9.47%)		NGT (WHO) N=3146 (67.27%)	
	MS + m ± s	MS - m ± s	MS + m ± s	MS - m ± s	MS + m ± s	MS - m ± s
Number of subjects (% of category)	773 (71.05%)	315 (28.95%)	310 (69.98%)	133 (30.02%)	1058 (33.63%)	2088 (66,37%)
Waist circumference (cm)	105.07±12.90	84.12±12.71	104.40±12.58	87.11±13.17	103.14±11.23	89.53±14.25
BMI (cm)	31.04±5.27	25,08±4.30	30.34±5.02	25.77±5.21	29.69±4.89	25.71±4.42
Waist/Height	63.94±8.28	49.91±7.17	63.47±7.65	52.45±8.45	62.53±7.35	53.94±8.88
Triglycerides (mg/dl)	181.54±150.37	127.44±148.66	166.95±108.94	111.28±75.60	177.45±115.80	108.12±84.34
Total cholesterol (mg/dl)	219.06±47.10	211.47±45.44	222.69±42.61	213.57±41.30	226.03±47.89	212.89±45.25
LDLc (mg/dl)	130.72±43.16	122.95±48.77	128.71±46.35	93.90±65.16	138.45±45.89	120.99±52.00
HDLc (mg/dl)	51.83±15.84	58.50±18.22	55.70±17.71	62.38±19.14	50.97±15.51	60.47±16.39

The acronyms are: DM (Diabetes Mellitus); IFG (Impaired Fasting Glycemia), NGT (Normal Glucose Tolerance), MS (Metabolic Syndrome). The statistics for the anthropometric measurements and biochemical parameters are presented as mean ± standard deviation, while for the number of subjects the percent values are calculated.

Table 2b. The analysis of variance (ANOVA) for the anthropometric measurements and biochemical parameters (WHO classification).

Total 2141 subjects with MS +	ANOVA		Post-hoc testing (Bonferonni)	
	F (df 2, 2512)	p	DM ↔ IFG p	DM ↔ NGT p
Waist circumference (cm)	5.94	0.003**	1.000	0.002**

BMI (cm)	15.91	<0.001**	0.125	<0.001**
Waist/Height	7.63	<0.001**	1.000	<0.001**
Triglycerides (mg/dl)	1.43	0.240	0.274	1.000
Total cholesterol (mg/dl)	4.94	0.007**	0.751	0.005**
LDLc (mg/dl)	9.34	<0.001**	1.000	0.001**
HDLc (mg/dl)	10.28	<0.001**	0.001**	0.758

The post-hoc testing was performed using the Bonferonni procedure. With * and ** we marked the statistically significant and very significant differences, respectively.

The glucose tolerance categories based on ADA criteria

The main characteristics of the study subjects, according to ADA criteria for glucose tolerance, are presented in Table 3a.

Changing the criteria for glucose tolerance does not modify the prevalence of MS in the sub-group with DM, but in the sub-group with IFG, 779 persons had MS, giving a prevalence of 63.44%, while to the people with NGT, the MS was present in 24.95% of cases.

Similarly to the previous analysis, we considered the subjects with MS as a sub-group of higher risk in all these three categories and applied the analysis of variance (ANOVA) to see whether there are any differences for the anthropometric measurements and biochemical parameters, and further applied the Bonferonni testing procedure for finding the pairs for which a statistically significant difference exists (Table 3b). We observed that, the differences between groups were extremely significant, excepting the total cholesterol, for which the differences were only statistically significant (Table 3b).

Table 3a. The main characteristics of the study subjects, according to ADA criteria for glucose tolerance.

Total 4677 subjects	DM (ADA) N=1088 (23.26%)		IFG (ADA) N=1228 (26.26%)		NGT (ADA) N= 2361(50.48%)	
	MS + m ± s	MS - m ± s	MS + m ± s	MS - m ± s	MS + m ± s	MS - m ± s
Number of subjects (% of category)	773 (71.05%)	315 (28.95%)	779 (63.44%)	449 (36.56%)	589 (24.95%)	1772 (75.05%)
Waist circumference (cm)	105.07±12.90	84.12±12.71	103.67±12.11	85.96±13.10	103.10±10.78	90.25±14.33
BMI (cm)	31.04±5.27	25.08±4.30	29.87±4.97	25.41±4.49	29.80±4.87	25.79±4.47
Waist/Height	63.94±8.28	49.91±7.17	62.76±7.78	51.28±8.07	62.73±6.94	54.51±8.93
Triglycerides (mg/dl)	181.54±150.37	127.44±148.66	159.14±98.95	115.87±94.09	196.14±129.04	106.39±80.94
Total cholesterol (mg/dl)	219.06±47.10	211.47±45.44	224.40±44.83	218.85±43.14	226.42±49.20	211.53±45.35
LDLc (mg/dl)	130.72±43.16	122.95±48.77	132.66±46.41	105.78±64.47	140.98±45.44	122.82±49.45
HDLc (mg/dl)	51.83±15.84	58.50±18.22	56.06±16.87	59.75±18.01	46.81±13.46	60.74±16.20

The acronyms are: DM (Diabetes Mellitus); IFG (Impaired Fasting Glycemia), NGT (Normal Glucose Tolerance), MS (Metabolic Syndrome). The statistics for the anthropometric measurements and biochemical parameters are presented as mean ± standard deviation, while for the number of subjects the percent values are calculated.

Table 3b. The analysis of variance (ANOVA) for the anthropometric measurements and biochemical parameters (ADA classification).

Total 2141 subjects with MS +	ANOVA		Post-hoc testing (Bonferonni)	
	F (df 2, 2512)	p	DM ↔ IFG p	DM ↔ NGT p
Waist circumference (cm)	4.98	0.007**	0.066*	0.009**
BMI (cm)	13.90	<0.001**	<0.001**	<0.001**
Waist/Height	5.87	<0.003**	0.008**	<0.013*
Triglycerides (mg/dl)	14.72	<0.001**	0.002**	0.110
Total cholesterol (mg/dl)	4.64	0.010*	0.075	0.012*
LDLc (mg/dl)	9.47	<0.001**	1.000	<0.001**
HDLc (mg/dl)	58.54	<0.001**	<0.001**	<0.001**

The post-hoc testing was performed using the Bonferonni procedure. With * and ** we marked the statistically significant and very significant differences, respectively

The arterial hypertension (HA) was also considered as a potential factor associated with DM and IFG. We found a very significant association between HA and the glucose tolerance categories, with higher percents of hypertensive subjects with DM and IFG (when compared with NGT), both for the ADA and the WHO classification criteria (Table 4).

Table 4. Association between arterial hypertension and the glucose tolerance categories, considered both for the ADA and the WHO criteria of classification.

		DM N (% of column)	**IFG (ADA) N (% of column)**	**NGT (ADA) N (% of column)**	**IFG (WHO) N (% of column)**	**NGT (WHO) N (% of column)**	**Total N (%)**
HTA	-	492 (46.5%)	531 (49.3%)	1365 (61.2%)	156 (41.2%)	1740 (59.4%)	2388 (54.7%)
	+	565 (53.5%)	547 (50.7%)	866 (38.8%)	223 (58.8%)	1190 (40.6%)	1978 (45.3%)
Total		1057 (100%)	1078 (100%)	2231 (100%)	379 (100%)	2930 (100%)	4366 (100%)
Person Chi-square test (2 df)			Chi-square=79.084 p<0.001 **		Chi-square=82.352 p<0.001 **		

The Pearson Chi-square test was applied to assess the statistical significance of the association observed, separately for the DM with ADA categories, and DM with WHO categories. The statistically very significant association was marked with **.

Discussion

In the adult population of Hunedoara county, the prevalence of MS, defined based on IDF 2005 criteria, was 45.78%, greater than those reported in western Europe and in surrounding counties. This may be explained by the characteristics of the study group, which had a mean age ~ 58 years and a great prevalence of overweight (39.47%) and obesity (29.05%), especially of central obesity (73.94%).

The most important identified risk factors for MS were the age, the abdominal obesity and sedentary lifestyle. The prevalence of MS was not significantly influenced by the gender in any age group, but was correlated with abdominal circumference, BMI and fasting glycemia. In the sub-group of DM, the prevalence of MS was even greater, 71.05%, while in the sub-group of IFG, this varied

according the criteria used to define it. From the people with central obesity (IDF 2005) 61.91% had MS.

The MS is not a clear clinical entity and that is why it should not be used as a clinical diagnosis. Central obesity and/or insulin resistance have been described as a key underlying components of the syndrome, but the exact etiology and pathogenesis of the condition is still unclear. It should be considered as only a premorbid condition which could find out, in epidemiological studies, the persons with DM and cardiovascular disease. Beside the central obesity and insulin resistance, there are a lot of other factors that contribute to the high risk of DM and CVD: modifications of the immune system, alterations of hypothalamus-hypophysis-suprarenal axis, changes in glucocorticoid actions, involvement of cytokines, hormones and other molecules produced by adipose tissue, HTA, alterations of blood lipids. While lifestyle and environment factors contribute to MS, there is also a genetic basis for the condition.

In the same time, the risk factors for DM and CVD, and different associations of them, are not equivalent. DM and CVD have multiple causes, some of them did not imply the MS, even if these ones can rise the risk of developing this syndrome. There are 16 different modes to define the MS according to Adult Treatment Panel III (ATP III) and 11 different modes based on IDF, and each combination of diagnostic criteria defines populations with different risk, making the epidemiological studies more difficult to design and interpret.

Although it is very important to identify the persons with MS, in order to control the existing cardio-metabolic risk factors, taking to the reduction of the risk for DM and CVD.

Conclusions

This study shows a high prevalence of MS in the examined population. It has some limitations. Being a cross-sectional study, the causal pathways could not be examined. The population is a community based sample and the subjects were not randomized. It's strength stays in the number of the sample that represents 1% of the Hunedoara county population.

Screening of asymptomatic adults for DM is controversial and is not cost-effective. The MS may be a good predictor of DM because of insulin resistance which is commonly associated with this clustering of metabolic factors and frequently precedes the onset of DM.

Our study may suggest that the burden of DM and CVD in Hunedoara county will increase as a consequence of a high rate of MS. That's why it is important that every effort should be made for the management of the MS, in order to reduce the risks of DM and CVDs in this population. Due to the high cardio-metabolic risk associated with MS primary prophylactic measures, screening and management protocols formulations must be imposed. For this it is necessary that every consultation, especially that of general practitioners, to include the measurement of height, weight, abdominal circumference and blood pressure.

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