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Prevalence of metabolic syndrome in normal weight individuals

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Abstract

Introduction and objective. The prevalence of metabolic syndrome and overweight in individuals with normal body weight is connected with higher exposure to type 2 diabetes and cardiovascular diseases. The aim of the study was to evaluate the risk and frequency of occurrence of metabolic syndrome and each of its components among individuals with normal weight.

Materials and method. Data were obtained by structured interview, and by measurements of anthropometric factors and blood analyses among 13,172 individuals aged 37–66. The risk of occurrence of metabolic syndrome was analysed in tertiles within the normal range of BMI (18.5–24.9 kg/m^2).

Results. Metabolic syndrome was diagnosed in 17.27% of individuals with normal weight. A significant increase in the risk of occurrence of metabolic syndrome in females was observed within the second (OR = 2.22; 95% CI: 1.63–3.05) and the third (OR = 3.97; 95% CI: 2.97–5.36) tertiles of normal BMI values. In males, a significantly higher risk of occurrence of metabolic syndrome was noted only in the highest BMI tertile (OR = 2.16; 95% CI: 1.26–3.83), compared to the reference level.

Conclusions. A high frequency of occurrence of metabolic syndrome risk factors was observed among individuals with BMI close to the upper cut-off point of the normal range. In order to early diagnose metabolically obese individuals with normal weight it is necessary to check the waist circumference when BMI ≥ 22.5 kg/m^2 in females, and BMI ≥ 23.8 kg/m^2 in males, where abnormal values should be a signal that further examinations should be performed to determine other risk factors of metabolic syndrome.

Key words

metabolic syndrome, risk factors, body mass index

INTRODUCTION

Over 30 years ago, metabolic disorders were observed in some patients with normal weight, similar to disorders which characterized obese individuals. Such patients were described as being a metabolically obese normal weight (MONW) phenotype [1]. In these individuals, an increase in visceral adipose tissue mass, fasting hyperglycemia, lower insulin sensitivity of target tissues, hyperinsulinemia, atherogenic dyslipidemia, high arterial pressure, fatty liver, and greater plasma proinflammatory cytokine concentrations are usually diagnosed [1, 3, 4]. Due to the lack of uniform criteria for identification of a MONW phenotype, and examination of different ethnic and age groups, it is difficult to make an actual assessment of the scale of the problem [1, 2, 3, 5, 6, 7, 8]. Megis et al. [3], in a longitudinal study, identified this syndrome only in 7.1% of those who had BMI < 25 kg/m^2. Pajunen et al. [9] confirmed the occurrence of MONW in 20.4% of males and 23.8% of females aged 45–74.

To-date, factors which are responsible for the occurrence of this condition have not been unequivocally defined. It has been suggested that low birth weight and low body mass in the first year of life may predispose to the accumulation of visceral adipose tissue in later life and, at the same time, may contribute to metabolic syndrome [1]. The effect of an inadequately balanced diet [4, 10], insufficient physical activity [1, 2, 10], low values of an upper limit of aerobic capacity (VO_2 max) and low post-exercise energy expenditure [10], as well as the role of genetic factors [1], are also emphasized. In individuals with MONW, a higher exposure to type 2 diabetes and cardiovascular diseases was observed [3–7, 10–12]. However, due to the low values of BMI, the risk of falling ill is, after all, underestimated both by doctors and patients. Early identification of individuals at risk is additionally hindered because of the lack of uniform diagnostic criteria of MONW. Therefore, this issue requires further examination. The objective of the study was to assess the frequency and risk of the occurrence of metabolic syndrome in normal-weight subjects. The analysis also covered the frequency of occurrence of abnormal values of each component of the metabolic syndrome according to the BMI.

MATERIALS AND METHODS

The research material was collected within the framework of the PONS (Polish-Norwegian Study) project. This is an open-ended prospective study aimed at the observation of the health state of inhabitants from the south-eastern part of Poland from the aspects of the morbidity and mortality rates due to cancer, cardiovascular diseases, and other main causes of morbidity and mortality. The research was conducted in the urban and rural environment of the Świętokrzyskie Province of Poland from September 2010 – October 2012. The study covered a population sample of 13,172 individuals (4,447 males and 8,725 females) aged 37–66; 388 of whom were excluded from the investigations because of the lack of complete data. The detailed information concerning the

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project, the research procedure and the way the study sample was selected, have been described in previously published reports [13].

Anthropometric measurements included height, weight, and waist circumference. BMI values between 18.5–24.9 kg/m^2 were considered as normal weight. The individuals with normal BMI were then divided into 3 tertile groups: T1=18.5–22.4; T2=22.5–23.7; T3=23.8–24.9 kg/m^2. Blood pressure was measured by means of the Omron M3 IntelliSense manometer. The level of glucose in blood serum was determined by an enzymatic method with hexokinaze, while the concentration of glycerides by means of oxidase of glycerophosphate and peroxidase. A total cholesterol level was determined by an enzymatic method with cholesterol esterase and oxidase, and the level of HDL cholesterol determined by the precipitation colorimetric method.

The prevalence of metabolic syndrome (MetS) was determined based on the recommendation of the International Diabetes Federation Task Force on Epidemiology and Prevention (joint interim statement in 2009) [14]. According to the established definition, metabolic syndrome was identified in persons who met at least 3 out of 5 criteria:

1) waist circumference ≥ 94 cm in males; ≥ 80 cm in females;
2) fasting glucose ≥ 100 mg/dl (5.5 mmol/l) or diabetes treatment;
3) triglycerides ≥ 150 mg/dL (1.7 mmol/l) or drug treatment for elevated triglycerides;
4) HDL cholesterol ≤ 40 mg/dL (1.0 mmol/l) in males; ≤ 50 mg/dl in females (1.3 mmol/l) in females or drug treatment for reduced HDL cholesterol;
5) systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg, or drug treatment for hypertension.

Metabolic obesity with normal body weight (MONW) was defined as the presence of at least 3 of 5 metabolic syndrome criteria and normal body weight (BMI=18.5–24.9 kg/m^2).

Into the confounding variables were classified the variables which exert an effect on the metabolic syndrome components, such as: age, education, place of residence, smoking, and leisure time physical activity. Two 15-year age intervals were distinguished: 37–51 and 52–66, 4 categories of education: elementary, vocational, secondary school and university education, as well as 2 categories of place of residence: urban and rural. Physical activity during leisure time was evaluated by means of the International Physical Activity Questionnaire (IPAQ). The respondents were divided into those who were active, i.e. fulfilling the recommendation: moderate-intensity aerobic physical activity for a minimum of 30 min. 5 days a week, or vigorous-intensity aerobic physical activity for a minimum of 20 min. 3 days a week, and those who were inactive, i.e. who did not meet the above-mentioned recommendations. The respondents who smoked every day during the period of study were considered as current smokers, those who ever smoked for a period longer than 6 months – as ex-smokers, while the remainder were considered as non-smokers.

Statistical analysis. Statistical analysis was performed using R Statistical Software, a free software environment for statistical computing and graphics, version 2.15.2. The prevalence of metabolic syndrome in the entire study group and in individuals with normal weight, according to gender, age, education level and a place of residence was analysed by means of the χ^2 (chi square) non-parametric test. Analysis of the frequency changes in the occurrence of individual risk factors of the metabolic syndrome in the BMI intervals was performed using the Mann-Whitney-Wilcoxon test. To assess the risk of occurrence of metabolic syndrome, according to the BMI categories, logistic regression was used. Risk ratios were adjusted for two confounding variables: age and education. The lowest tertile (T1) of normal BMI values constituted the reference level (OR 1.00). The p values $p<0.05$ were considered statistically significant.

RESULTS

For the analysis, 12,784 individuals (4,323 males and 8,461 females) were qualified for whom complete data were available. Table 1 shows the numerical characteristic of the study group. The largest number of respondents were rural inhabitants aged 52–66, who had a secondary education; women constituted 66.2% of the study group. The respondents were characterized by elevated average values of the BMI and waist circumference (Tab. 2). Males were also characterized by relatively high arterial systolic pressure.

Table 1. General description of population sample in the study

Socio-demographic variables	Categories	Males N = 4323		Females N = 8461		Total N = 12,784	
		n	%	n	%	n	%
Age	37 – 51	1,025	23.71	2,131	25.19	3,156	24.69
	52 – 66	3,298	76.29	6,330	74.81	9,628	75.31
Education	Elementary	299	6.92	831	9.82	1,130	8.84
	Vocational	1,298	30.03	1,383	16.35	2,681	20.97
	Secondary	1,686	39.00	3,984	47.09	5,670	44.35
	University	1,040	24.06	2,263	26.75	3,303	25.84
Place of residence	Rural	2,638	61.02	5,277	62.37	7,915	61.91
	Urban	1,685	38.98	3,184	37.63	4,869	38.09

Table 2. General description of risk factors of metabolic syndrome in the study population sample

Risk factors	Males		Females	
	X±SD	Median	X±SD	Median
Body Mass Index (kg/m^2)	28.5±4.0	28.2	28.0±5.0	27.3
Waist Circumference (cm)	99.3±10.4	99.0	88.2±11,9	87.0
Fasting glucose (mg/dL)	102.7±21.2	98.0	96.0±20,9	93.0
Triglycerides (mg/dL)	138.5±115.8	115.0	113.6±64,8	99.0
HDL cholesterol (mg/dL)	52.6±13.1	51.0	62.2±14.4	61.0
Systolic blood pressure (mmHg)	142.7±19.3	141.0	135.1±18.9	133.0
Diastolic blood pressure (mmHg)	84.9±10.9	84.0	81.0±10.3	80.5

Metabolic syndrome (at least 3 out of 5 criteria) occurred in 47.2% of the total number of individuals examined, significantly more often among males than females, and in respondents aged 52–66, compared to the younger age group (Tab. 3). It occurred most rarely in individuals who had a university education; however, no significant differences were observed between the place of residence. Metabolic syndrome was also significantly more often diagnosed in respondents who did not meet the recommendations concerning physical

Table 3. Prevalence of metabolic syndrome (at least 3 out of 5 criteria) among all respondents and in normal weight individuals (MONW) (%)

Variables	Categories	Prevalence of metabolic syndrome			
		among all respondents		in respondents with normal BMI	
		Males	Females	Males	Females
Gender		53.83***	43.79***	16.71 NS	17.44 NS
Age	37 – 51	44.88***	10.33**	10.33**	9.69***
	52 – 66	56.61	19.28	19.28	21.77
Education	elementary	53.85*	6.52*	6.52*	31.20***
	vocational	54.24	15.17	15.17	20.07
	secondary	55.87	21.99	21.99	19.11
	university	50.00	13.30	13.30	12.41
place of residence	rural	52.52 NS	15.93 NS	15.93 NS	17.64 NS
	urban	54.66	17.16	17.16	17.36
physical activity	active	47.39*	37.94*	10.91 NS	15.82 NS
	inactive	54.37	44.12	17.18	17.55
Smoking	current smokers	51.17***	43.75 NS	18.01**	21.06*
	ex-smokers	60.93	44.51	22.75	17.09
	non-smokers	46.73	43.4	10.42	15.75

* – statistically significant difference at the level $p < 0.05$,
** – statistically significant difference at the level $p < 0.01$,
*** – statistically significant difference at the level $p < 0.001$,
NS – non-significant

activity, compared to those who were active, and in the case of males – more often among ex-smokers and current smokers, compared to non-smokers. The criteria of MetS were met by 17.27% of the respondents with a normal weight (BMI=18.5–24.9 kg/m^2).

Metabolic syndrome classified as MONW prevailed with similar frequency in both genders, but twice as often in the older age group. In the group of females, MONW occurred the most rarely in those with university education, whereas among males – in the group of those who had completed elementary education. MONW was also slightly more frequently diagnosed in respondents who did not fulfil the recommendations concerning physical activity, compared to those who were active; however, the differences observed were statistically insignificant. Significant differences were noted between the occurrence of MONW and smoking. The percentage of respondents with this syndrome was considerably higher among males and females who were ex- and current smokers, than in the group with normal BMI without the syndrome.

Analysis of individual risk factors of the metabolic syndrome in respondents with normal weight showed that, both in males and females, the frequency of the occurrence of abnormal waist circumference increased significantly with an increase in the BMI (Tab. 4). On the level of the second tertile of normal BMI values, a more than 3-fold increase was found in the frequency of occurrence of excessive weight circumference, compared to the lowest, reference tertile. On the level of the third tertile, a more than 5-fold increase in the occurrence of abnormal waist circumference was noted among females, and more than 7-fold in males.

It was observed that with an increase in the BMI value, there was a significant increase in the prevalence of abnormal levels of HDL cholesterol and triglycerides in both genders, whereas among females a significant increase

Table 4. Percentage of respondents with abnormal values of individual risk factors of metabolic syndrome in a given BMI tertile.

Risk factors	Gender	BMI (18.5 – 24.9 kg/m^2)		
		T1	T2	T3
Waist Circumference	Male***	2.78	8.52	19.76
	Female***	10.45	32.38	56.07
Fasting glucose	Male NS	32.22	26.91	29.50
	Female **	10.68	12.95	16.50
Triglycerides	Male **	8.89	16.14	17.70
	Female **	7.04	10.49	12.14
HDL cholesterol	Male *	3.89	6.28	10.32
	Female ***	7.75	9.84	15.29
Systolic blood pressure	Male NS	62.78	60.09	61.95
	Female *	41.90	44.04	49.03
Diastolic blood pressure	Male NS	34.44	30.49	35.40
	Female NS	21.83	23.58	26.09

* – statistically significant at the level $p < 0.05$
** – statistically significant at the level $p < 0.01$
*** – statistically significant at the level $p < 0.001$
NS – non-significant

in the prevalence of abnormal values of glucose level and systolic blood pressure was found. No significant changes were observed only with respect to the values of diastolic blood pressure. However, it is noteworthy that the percentage of respondents with abnormal values of both systolic and diastolic blood pressure (or taking medication for high blood pressure – hypertension) was also quite high in individuals with the lowest BMI (18.5–22.4 kg/m^2).

A significant increase in the risk of occurrence of metabolic syndrome in the females could be observed already in the second tertile of the normal BMI values (Tab. 5). In males, a significantly higher risk of the occurrence of metabolic syndrome was reported only in the group of males in the highest, third BMI tertile.

Table 5. Frequency and risk of occurrence of metabolic syndrome in normal-weight individuals according to BMI category (OR adjusted for age, education, smoking and physical activity)

BMI	Males (N = 124)			Females (N = 427)		
	%	OR (95% CI)	p	%	OR (95% CI)	p
T1	16.13	1.00	-	16.86	1.00	-
T2	24.19	1.18 (0.62–2.21)	0.6094	30.45	2.22 (1.63–3.05)	0.0000 p<0.001
T3	59.68	2.16 (1.26–3.83)	0.0063 p<0.01	52.69	3.97 (2.97–5.36)	0.0000 p<0.001

DISCUSSION

Metabolic syndrome, i.e. an occurrence of at least 3 out of 5 criteria, recommended by the International Diabetes Federation Task Force on Epidemiology and Prevention (joint interim statement in 2009) [14], were reported in 47.2% of the total number of respondents (53.38% of males; 43.79% of females). An increased risk of metabolic syndrome occurred at the BMI ≥ 22.5 kg/m^2 in females, and the BMI ≥ 23.8 kg/m^2 in males. In previous Polish studies, metabolic syndrome – defined according to the IDF – was diagnosed

in 30.75% of males and 26.8% of females. However, these studies concerned a much younger population, starting from the age of 20 [15]. In Wrocław, Poland, metabolic syndrome was diagnosed in 12.7% of 40-year-old females, and in 33.1% of 50-year-old females, and in males, in 30.4% and 42.1%, respectively [16]. Such a high percentage of individuals with metabolic syndrome reported in own studies resulted mostly from the sample selection. It was an open research; therefore, the study group could have covered an overrepresentation of individuals in whom the frequency of occurrence of metabolic syndrome risk factors was higher than in the general population. In addition, among the respondents dominated those aged 52–66. According to the result of studies conducted in the USA, the occurrence of metabolic syndrome increases together with age, from 6.7% in the age group 20–29 to 43.5% in the age group 60–69, and 42% in the group of individuals aged 70 and over [17].

In the group of those who had normal weight, 17.27% met the criteria of metabolic syndrome. This percentage should be considered as relatively high, considering the accepted definition of the syndrome, i.e. BMI<25.0 kg/m^2, but not <26–27 kg/m^2 as adopted by many other researchers [2, 6]. Meigs et al. [3] found this disorder in only 7.1% of those with the BMI < 25 kg/m^2. However, they applied the definition of metabolic syndrome according to the Third Report of the National Cholesterol Education Programme (ATP III); therefore, adopted the waist circumference – >102 cm for males and >88 cm for females. According to the data by Milewicz et al. [18], the frequency of the occurrence of MONW in postmenopausal women with normal body weight was 13.9%. Similar results were obtained in the Chennai Urban Rural Epidemiology Study, in which 15.1% of individuals with MONW [7] were identified by using the criteria according to South Asian Modified National Cholesterol Education Programme. Both in the study group and among those with a normal body weight, metabolic syndrome occurred most rarely in females with university education. Studies by many researchers have shown that the frequency of occurrence of health problems was higher in individuals who had only elementary education, a lower position at work and low income [19, 20, 21].

Recently published findings of long-term studies confirmed that the risk of the occurrence of type 2 diabetes was the highest in the group with the lowest social status, and almost a half of the social inequality in the frequency of the occurrence of this disorder was explained by modifiable risk factors, including such health behaviours as: smoking, alcohol consumption, inadequate diet, physical activity, as well as obesity [22]. The relationship between education and the frequency of the occurrence of metabolic syndrome in males was not as well defined as that for females. The lowest percentages of respondents with metabolic syndrome were reported in the group of those with university education; however, this syndrome occurred relatively rarely in the group of those who completed only elementary education. This may be related with differences in health status and health behaviours between Polish males and females, which have been often observed [23]. This phenomenon was confirmed by the research findings of Alves et al. [21]. Among females, the frequency of the occurrence of the majority of risk factors was higher in the group with the lowest status.

In males, similar to the presented study, it was found that the socio-economic gradient of the risk factors analysed was less clear, although also in the study [21], a lower socio-economic status was associated with more frequent alcohol abuse and a higher frequency of the occurrence of type 2 diabetes. According to the above-mentioned researchers, a clearer relationship between the social status and risk factors in females suggested that the adoption and use of health promoting behaviours by females, to a greater extent, is dependent on the financial and symbolic factors than among males.

In males, an increase in the BMI value above the first tertile was accompanied by a significant increase in the occurrence of abnormal values of only 3 risk factors of metabolic syndrome, i.e., waist circumference, HDL cholesterol and triglycerides. Among females, an increase in the BMI resulted in a significant growth in the frequency of occurrence of abnormal values of nearly all the risk factors (except diastolic blood pressure). Beigh and Jain [24] confirmed that individual risk factors of metabolic syndrome may differ between males and females and, therefore, contribute to gender-related differences in the risk of metabolic complications, such as insulin resistance. Despite the fact that the total frequency of occurrence of MONW was similar in both genders, an increased risk of this syndrome was noted among females with considerably lower BMI values. Within the second BMI tertile (22.5–23.7 kg/m^2) more than 32% of respondents had abnormal values of waist circumference, whereas in the third tertile (23.5–24.9 kg/m^2) – more than a half (56%). An increased risk of metabolic syndrome in males occurred only in the third BMI tertile – in this group nearly 20% of respondents had an abnormal waist circumference.

Metabolic obesity in individuals with normal weight is a serious health problem due to the high risk of the development of type 2 diabetes and cardiovascular diseases, compared to those with similar BMI but without symptoms of metabolic syndrome [3, 4, 5, 10, 11, 12, 24]. Although in respondents with MONW the relative risk of cardiovascular diseases was lower than in those obese with metabolic disorders, it was 2–3 times higher than in healthy individuals [4]. Romero-Corral et al. [5] also showed a higher mortality due to cardiovascular diseases in females. Hadaegh et al. [11] reported a 3–9 times higher risk of the occurrence of diabetes in individuals with a normal body weight and the metabolic syndrome phenotype, compared to those with normal body weight, but without metabolic syndrome. In a longitudinal research, Meigs et al. [3] found that in patients with MONW the frequency of occurrence of type 2 diabetes reached 3%, while in the group of non-obese healthy individuals (BMI<25 kg/m^2) this disease occurred more rarely, i.e. in 1.2%. Ärnlöv et al. [25] observed that among males with a normal body weight and metabolic syndrome the risk of occurrence of diabetes was 3 timed higher, compared to those with a normal body weight and without the syndrome.

The presented study also has some limitations. Firstly, the study group was not selected at random. Hence, the number of males was considerably lower than that of females, who happened to be more interested in the examination of their state of health. Secondly, in the analysis of results, certain confounding factors were not considered which might have exerted an effect on the occurrence of risk factors of metabolic syndrome, such as the consumption of nutrients. The advantage of the analysis performed is primarily the consideration, while defining metabolic obesity with a regular weight (MONW), of the BMI values which are commonly

accepted worldwide as normal (18.5–24.9 kg/m^2), in contrast to the higher values of this index, arbitrarily adopted in many other studies. The strong point of this research is also the fact that the study covered a large population sample (N=13,172).

CONCLUSIONS

The results of the study show that metabolic syndrome was significantly more frequent in males within the highest tertile, and in females within the second and third normal BMI tertile, compared to those within the lowest, first tertile. Due to the possession of body weight within the commonly accepted range many patients with MONW for a long time remain undiagnosed and are not aware of the increased risk of type 2 diabetes and cardiovascular diseases, as well as the necessity for the implementation of changes in life style, or possibly a pharmacological treatment. They are not covered by any preventive programmes. Due to the need for the earliest possible diagnosis and screening of individuals with MONW, the measuring of waist circumference should be recommended when BMI≥22.5 kg/m^2 in females and BMI≥23.8 kg/m^2 in males, and abnormal waist size should be a signal for performing further examinations in order to determine other risk factors of metabolic syndrome.

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