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LETTER TO THE EDITOR

Metabolically healthy obese and metabolically unhealthy non-obese phenotypes in a Russian population

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Abstract

Introduction The aim of the study was to estimate the prevalence of metabolically healthy obese (MHO) and metabolically unhealthy non-obese (MUNO) phenotypes in Russian population.

Design and methods In cross-sectional epidemiology survey "Epidemiology of cardiovascular diseases and its risk factors in some regions of the Russian Federation" a random sampling of 21,121 subjects (25–65 years), stratified by age and sex was involved. Anthropometry, blood pressure (BP) measurement and fasting blood-tests (glucose, lipids) were performed according to standard protocols. Criteria for MHO—body mass index (BMI) $\geq$30 kg/m^2 and $\leq$2 of markers: HDL < 1.30 (females)/1.04 (males) mmol/l; triglycerides $\geq$1.7 mmol/l; glucose $\geq$5.6 mmol/l or treatment; waist >88 (females)/102 (males) cm and BP $\geq$ 130/85 mm Hg or therapy. Criteria for MUNO was BMI < 30 kg/m^2 and $\geq$2 markers listed above. Simple tabulations, descriptive statistics, post-stratification weights and logistic regression were used for analyses.

Results MHO phenotype was detected in 2856 (41.5%) obese people; MUNO phenotype—in 4762 (34.4%) non-obese subjects. Aging was negatively associated with MHO and positively with MUNO prevalence. Gender was registered as determinant only of MUNO probability. No dramatic differences in lifestyle risk factors between 3 BMI groups (lean, overweight, obese) were found out.

Conclusion Half of obese Russian inhabitants are metabolically healthy. At the same time, metabolic abnormalities were detected in one third of non-obese participants with a shift to male gender.

Keywords Obesity · Metabolic health · Metabolically healthy obesity · Russian population

Obesity is one of the most important public health challenges of the twenty-first century. It is known, that overweight and obesity are closely related to the onset and progression of cardiovascular disease, type 2 diabetes and several types of cancer [1]. However, it is also obvious that not all obese individuals are at increased risk of cardiovascular and metabolic complications—later are considered "metabolically healthy" people with obesity [Metabolically Healthy Obese (MHO)]. MHO phenotype can be characterized by normal insulin sensitivity, lipid profile, blood pressure and inflammation markers profile despite elevated fat mass [2]. Conversely, non-obese subjects can demonstrate "unhealthy" metabolic profile [Metabolically Unhealthy Non-Obese (MUNO)] that may be associated with higher risk of chronic non-communicable diseases [3].

Currently no clear picture of these phenomena was obtained. Moreover, the data on MHO or MUNO phenotype prevalence in Russian population is lacking. The aim of the study was to estimate the prevalence of metabolically healthy obesity and metabolically unhealthy non-obese phenotypes in Russian population.

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This was cross-sectional multicentre population-based study called “Epidemiology of cardiovascular diseases and its risk factors in some regions of the Russian Federation—ESSE-RF”. The study based on the data from 13 country regions located in different parts of Russia: North Ossetia—Alania (North Caucasus), Volgograd (South), Vologda (North-West), Voronezh (Centre), Ivanovo (Centre), Kemerovo (West Siberia), Krasnoyarsk (East Siberia), Orenburg (Volga region), Vladivostok—Primorsky krai (Far East), Samara (Volga region), Saint-Petersburg (North West), Tomsk (West Siberia), Tyumen (Ural).

The sample of the survey was multi-stage clustered, and formed by Kish method. Participants with malignancy, significant chronic liver disease, chronic kidney disease and those lacking data for variables were excluded.

The survey was accomplished between 1 November 2012 and 25 November 2014. The study protocols were approved by Ethics Committees of National Research Centre for preventive Medicine (Moscow), Russian Cardiology Research and Producing Centre (Moscow) and Federal Almazov North-West Medical Research Centre (Saint-Petersburg) and written informed consent was provided by each participants.

The office resting blood pressure (BP) measurement was performed in a supine after 5 min of rest on the right upper arm using a calibrated digital electronic device (Omron, Japan) with an appropriately sized cuff. The levels of systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured twice and the average level was calculated.

Anthropometry was performed in accordance with standard procedure. Height (accuracy up to 0.5 cm, in the standing position, by stadiometer Medical RP (TVES, Russia), weight (accuracy up to 100 g, by medical scales HEM-150 MASSA-K, Russia) and waist circumference (WC) were measured. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). All individuals were grouped according to BMI in normal weight (BMI < 25 kg/m^2), overweight ($30 >$ BMI ≥ 25 kg/m^2) and obese (BMI ≥ 30 kg/m^2) groups. Underweight individuals (BMI ≤ 18.5) were excluded from analysis.

All participants filled in a questionnaire regarding marital status, smoking, physical activity, alcohol and fruits/vegetables intake. Subjects were considered as physically active if they were moving more than 300 min/week.

Fasting serum total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), triglycerides (TG), glucose concentrations were conducted at auto-analyser ARCHITECT (USA) and reagent kits (Abbott).

Criteria for metabolic health [4] were applied: HDL < 1.30(F)/1.04 (M) mmol/l; triglycerides ≥ 1.7 mmol/l; glucose ≥ 5.6 mmol/l or treatment; WC > 102(M)/88 (F) cm and BP $\geq 130/85$ mm Hg or therapy. Obese subjects (BMI ≥ 30 kg/m^2) were classified as MHO (≤ 2 of markers of metabolic health) and MUO (metabolically unhealthy obese); non-obese subjects (BMI < 30 kg/m^2) were classified as MHNO (metabolically healthy non-obese) and MUNO (≥ 2 markers of metabolic health).

The sex- and age-specific characteristics of the sample were obtained by simple tabulations and descriptive statistics. For behavioural and biomedical variables, these parameters were calculated from the weighted data, using post-stratification weights that were adjusted for European standards. The associations and covariates of interest were assessed in logistic regression analyses. All statistical analyses were performed using SPSS 17.0 (USA).

Final sample included 7834 males (37.7%) and 12946 females (62.3%) aged 25–65 years (mean age was 46.4 ± 0.8 years); among them 6881 (32.6%) were obese and 13899 (67.4%)—non-obese subjects (according to BMI). MHO phenotype was detected in 2856 (41.5%) obese: 915 (43.0%) males and 1941 (40.9%) females, $p = 0{,}053$. MUNO phenotype had 4762 (34.4%) non-obese subjects: 2055 (35.4%) males and 2707 (32.5%) females, $p < 0.001$. The majority of MUNO subjects (75.3%) comprised overweight group.

Smoking was associated with unhealthy metabolic profile in lean subjects (BMI < 25 kg/m^2). Among MHO and MUO participants no significant lifestyle differences were found out. Alcohol consumption was comparable in all groups—data is shown in Table 1.

Multivariable logistic regression demonstrated determinants of MUNO: age 1.06 [1.05; 1.07] and gender (females had significantly lower probabilities—OR 0.78 [0.72; 0.84] adjusted for age). The age was significant determinant of MHO presence—OR 0.96 [0.95; 0.97], $p < 0.001$.

This is the first population-based study that assessed prevalence of MHO and MUNO phenotypes in Russian Federation. The major result of the study is that less than half of obese Russian inhabitants are metabolically healthy. At the same time, metabolic abnormalities in non-obese subjects were detected in one-third of non-obese participants with a shift to male gender.

In 1973–1980, Keyes and Reuben Andres suggested that obesity could in some cases be benign and have no contribution to cardiovascular risk [5]. During that period, initial attempts to specify criteria for MHO and MUNO phenotypes were made. However, so far it is not clear what factors determine the metabolic health in obese subjects, and no common definition of “metabolically healthy obesity” exists. Currently to assess the metabolic health in obese patients, most authors use metabolic syndrome criteria, including insulin resistance and systemic inflammation. In general, metabolic health criteria may be taken as more accurate cardiovascular risk marker rather than BMI.

Table 1 Sample characteristics as a function of metabolic health status and body mass index

	Metabolically healthy participants			Metabolically unhealthy participants		
	Normal weight	Overweight	Obese	Normal weight	Overweight	Obese
n	5324	3813	2856	1176	3586	4023
Age, years	39.5 (11.3)	44.6 (11.3)	49.1 (10.3)	46.26 (12.2)	50.4 (10.3)	52.9 (8.8)
25–34 years, n, %	2341 (43.9%)	1022 (26.8%)	353 (12.4%)	286 (24.4%)	417 (11.6%)	231 (5.7%)
35–44 years, n, %	1227 (23.1%)	807 (21.2%)	546 (19.1%)	206 (17.5%)	506 (14.1%)	452 (11.2%)
45–54 years, n, %	1044 (19.6%)	1092 (28.6%)	915 (32.0%)	299 (25.4%)	1169 (32.6%)	1284 (31.9%)
>55 years, n, %	712 (13.4%)	892 (23.4%)	1042 (36.5%)	385 (32.7%)	1494 (41.7%)	2056 (51.2%)
Males, n (%)	1843 (34.6%)	1860 (48.8%)	915 (32.0%)	508 (43.2%)	1547 (43.1%)	1214 (30.2%)
Married/cohabiting, n (%)	3180 (59.7%)	2591 (68.0%)	1885 (66.0%)	737 (62.7%)	2349 (65.5%)	2584 (64.2%)
Never smokers, n (%)	3206 (60.2%)	2156 (56.5%)	1883 (66.0%)	663 (56.4%)	2081 (58.0%)	2658 (66.1%)
Physically active, n (%)	1535 (28.8%)	1120 (29.4%)	874 (30.6%)	370 (31.5%)	1077 (30.0%)	1187 (29.5%)
≥1 fruit and vegetable/day, n (%)	3048 (57.3%)	2214 (58.1%)	1774 (62.1%)	664 (56.5%)	2163 (60.3%)	2554 (63.5%)
No alcohol, n (%)	1277 (23.9%)	915 (23.9%)	723 (25.3%)	286 (24.3%)	682 (24.8%)	1005 (24.9%)
Triglycerides, mmol/L,	0.9 (0.4)	1.1 (0.5)	1.3 (0.7)	1.7 (1.1)	1.9 (1.1)	2.2 (1.4)
HDL-cholesterol, mmol/L	1.6 (0.4)	1.5 (0.3)	1.4 (0.3)	1.3 (0.4)	1.3 (0.3)	1.2 (0.3)
LDL-cholesterol, mmol/L	3.1 (0.9)	3.4 (1.0)	3.5 (1.0)	3.4 (1.1)	3.6 (1.1)	3.6 (1.0)
Fasting glucose, mmol/L	4.8 (0.7)	4.9 (0.7)	5.0 (0.9)	5.7 (1.7)	5.7 (1.8)	6.2 (2.3)
Systolic blood pressure, mm Hg	121.6 (14.9)	127.5 (16.2)	135.0 (19.0)	126.0 (19.0)	140.0 (18.8)	147.0 (21.0)
Diastolic blood pressure, mm Hg	75.6 (9.4)	79.1 (9.7)	83.7 (11.0)	81.0 (11.7)	86.0 (10.5)	89.1 (11.6)

Values are mean (SD) unless otherwise indicated

Prevalence of metabolic health in the obese population can vary from 10% to almost 50%. MHO and MUNO phenotypes prevalence depends on diagnostic criteria. For example, in a study involving 2040 inhabitants of Ireland, 30.2% of obese subjects had MHO phenotype and 32.4% of non-obese—MUNO phenotype (according to Meigs criteria); in a Spanish study with 3844 participants—39.9% obese were MHO (according to Joint Interim Statement criteria of the metabolic syndrome) [6].

Little is known concerning MHO in Russia, the present study is the first one that is performed in a population-based sample. Recently it has been shown that only 8.7% of patients with abdominal obesity do not have insulin resistance or any additional metabolic syndrome component according to IDF criteria [7]. The prevalence of MHO and MUNO phenotype in Russian Federation seems to be the same compared to European and North America populations. Data on association between metabolic phenotype and age seems to be controversial. Yoo et al. [8] found no relation between age and metabolic profile among obese and non-obese subjects, while Gonçalves et al. [9] showed a decrease of MHO prevalence with age. According to our data, the proportion of MHO subjects was highest in youngest group with further progressive decline with age. Surprisingly, no dramatic differences in lifestyle risk factors between three BMI groups were found out, while other papers show better health behavior in terms of smoking, alcohol, and fruit and vegetables consumption in subjects with better metabolic profile [10].

One should remember that MHO and MUNO phenomena and weakness of BMI or WC criteria for obesity diagnosis might also be explained by inability to determine adipose tissue dispersion. A subcutaneous fat may be common for MHO phenotype; while central fat distribution closer to internal organs for MUNO.

The major limitation of the present study is its methodology. Since the study was a large population survey, we had no possibility for fat tissue volume assessment, as well as its body distribution measurement. Perhaps, subcutaneous and visceral fat measurement could be critical to determine metabolic health. In the present study, we did not measure CRP level and insulin resistance, thus, indicating metabolic health is diagnosed only according to standard lipid and glucose measurements.

A considerable number of obese patients are metabolically healthy (less than half) and on the contrary,—a significant portion of non-obese subjects are metabolically unhealthy (one-third) in Russian population. Lean metabolically unhealthy subjects should be revealed and informed for well-timed cardiovascular risk prevention.

Compliance with ethical standards

Conflict of interest No potentially competing interests are declared.

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