Gender differences in lipid metabolism of the young patients with metabolic syndrome longtime living in the North

Elena Victorovna Korneeva, Natalia EvgenjevnaTrekina, Alla Victorovna Rudenko

Surgut State University, Lenina Street, 1, Surgut, 628412, Russia

Abstract. With the growth in the length of stay in the North increases the body need for energy and nutrients. Balanced diet is an important factor of human adaptation in the North. One of the alimentary significant factors in the development of obesity and MS is a disorder of eating behavior, which particularly affects the willingness of patients to be ready to conduct medical measures. About insufficient saturation of the organism shows an abnormal increase in serum ghrelin among patients with MS. There were also sex differences in the changes of lipid profile among 366 patients with metabolic syndrome. Logistic regression showed a difference in the correlations between the parameters of lipid metabolism, testosterone, leptin in serum among men and women. Bad normalization of serum lipid parameters among women is associated with more frequent presence of leptin resistance than men.
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Introduction

A "northern" type of metabolism with the increasing of the fat and the proteins consumption is formed for the best adaptation of the longtime living in the North population [1, 2]. The indigenous population of the Khanty-Mansiysky autonomous district has been eaten the meat with the exogenous fat with a large amount of unsaturated fatty acids. It ensures a high rate of oxidation of lipids and defines the low level of the cholesterol. The eating disorders contribute to the formation of dislipidemia, obesity, hypertension, diabetes and metabolic syndrome (MS) [2].

In 2011 in the Khanty-Mansiysky autonomous district registered 176279 people with diseases circulatory system. Ever year about 30 000 new cases happens to diseases of the heart and blood vessels. Mortality rate of cardiovascular diseases was 301.6 per 100 000 population, which was 2.5-3 times higher than of other reasons [3]. Many scientists believe that the cardiovascular system of the alien population is a more aggressive and develops an average on 10-15 years earlier than the population of the middle latitudes [4]. In the peculiarities the formation of obesity, MS, hypertension sex hormones play an important role. These gender differences are typical for young and middle-aged patients. Determine the differences among older patients is difficult, as they have age-related changes and other somatic diseases. This prospective study of lipids in the blood serum of 366 patients with metabolic syndrome evaluates the correlation between the changes of the blood lipid, testosterone, leptin, ghrelin in serum among men and women and the duration of life in the North .

Methods

366 patients with metabolic syndrome (188 women and 178 men, with average age 36.21±0.46 18 40 years) were examined in Clinical city hospital # 1 and in District cardiology clinic Diagnostic Center and Cardiovascular Surgery in city Surgut, in Russia. This study was performed in accordance with the ethical standards. The basic sign of the metabolic syndrome is waist circumference (WC) more than 80 cm by women and more than 94 cm by men (the central (abdominal) type of obesity). Additional criteria are hypertension (BP ≥ 130/85), elevated triglycerides (TG)((≥1.7 mmol/L), lowering of high density lipoprotein cholesterol (HDL-C) (<1.0 mmol/L men, <1.2 mmol/L women), increasing of low density lipoprotein cholesterol (LDL-C) > 3.0 mmol/L, very low density lipoprotein cholesterol (VLDL-C) (0,13 - 1,63 mmol/L), total cholesterol (TC) (3.50 – 5.20 mmol/l), hyperglycemia (fasting glucose in plasma on an empty stomach ≥ 6.1 mmol/L), impaired glucose tolerance (glucose in plasma 2 hours after glucose load within ≥ 7.8 and ≤ 11.1 mmol/L). The presence of the patient's central obesity and two additional criteria are the basis for the diagnosis of the metabolic syndrome. The exclusion criteria were the cancer, psychiatric illness, hepatitis B or C. In the control group was observed 130 people (68 women and 62 men, with mean average 30.84±0.90). They were comparable to gender, length of residence in the North with the group of patients with the metabolic syndrome. We conducted a survey

of all the surveyed men and women to assess eating behavior by using questionnaire DEBQ.

We measured the weight, the height, BMI, the blood pressure. To evaluate the lipid, carbohydrate and hormonal profiles of patients we took the blood from the cubital vein no earlier than 12 hours after the last meal. Level of ghrelin was examined at 2 hours after a meal. Blood lipids were measured with the «Vitalab Flexor» device (USA) using reagents of the company «La Roche»: HDL and low-density (HDL-C, LDL-C) with the homogeneous method, total cholesterol (TC) and triglycerides (TG) with the colorimetric method. Measurement of serum hormone was performed with immunohemilyuminescence method on an automated analyzer "Arthitest" (USA) using reagents firm "Abbot" (USA).

The statistical program STATISTICA7 was used to perform statistical analysis. The critical level of statistical meaning in testing the null hypothesis was assumed 0.05. To analyze the correlation between serum lipid and hormones parameters, length of residence in the North and the onset of metabolic syndrome was carried a logistic regression model with a stepwise algorithm for inclusion and exclusion of predictors.

Results and discussion

The majority patients of the clinical group (136 people - 37.2%) lived in the North 17.4 ± 1.25 years. 90 (69.2%) of surveyed men and women of the control group lived in the Khanty-Mansiysky autonomous district 18.2 ± 1.15 years. At the beginning of the study 104 patients (28.4%) (38.3% women and 18.0% men) lived in the North up to 3 years. In the northern conditions up to 10 years lived 126 (34.4%) patients (41.5% women and 27.0% men) (table 1).

All surveyed men and women of the control group had the normal weight.

Table 1. The obesity frequency of the young working population (%) longtime living in the North

BMI kg/m²	The duration of the living in the North		
	up to 3 years	up to 10 years	more than 10 years
	Women		
The clinical group			
The overweight (25.0-29.9)	24(25.53%)	23(24.47)	3(3.19%)
The obesity I (30.0-34.9)	-	6(6.38%)	10(10.64%)
The obesity II (35.0-39.9)	-	3(3.19%)	4(4.26%)
The obesity III (≤ 40)	-	-	2(2.13%)
The normal weight (18.0-24.9)	12(12.77%)	7(7.45%)	-
The control group	5(14.71%)	7(20.59%)	22(64.71%)
	Men		
The clinical group			
The overweigth (25.0-29.9)	2(2.25%)	7(7.87%)	21(23.60%)
The obesity I (30.0-34.9)	4(4.49%)	4(4.49%)	10(11.24%)
The obesity II (35.0-39.9)	3(3.37%)	3(3.37%)	6(6.74%)
The obesity III (≤ 40)	-	-	1(1.12%)
The normal weight (18.0-24.9)	7(7.87%)	10(11.24%)	11(12.36%)
The control group	3(9.68%)	5(16.13%)	23(74.19%)

Table 2. The average of serum lipid, leptin and ghrelin data of MS groups is higher than in the control group (M±m)

	Normal range	MS women group (n=188)	Control group (n=68)	MS men group (n=178)	Control group (n=62)
TC (mmol/L)	3.50 – 5.20	5.86 ± 0.06	4.45 ± 0.04	6.12 ± 0.02	4,45 ± 0,04
TG(mmol/L)	0.00-1.70	3.37 ± 0.08	0.93 ± 0.01	4.62 ± 0.01	1,60 ± 0,02
HDL-C(mmol/L)	0.90-1.90	0.83 ± 0.02	1.75 ± 0.01	1.72 ± 0.01	1,92 ± 0,02
LDL-C(mmol/L)	0.00-3.50	4.02 ± 0.05	2.72 ± 0.01	6.22 ± 0.04	3,02 ± 0,01
VLDL- C (mmol/L)	0,13 - 1,63	2.05 ± 0.02	0.38 ± 0.01	3.92 ± 0.01	1,08 ± 0,01
TG/HDL-C	<1.5	3.10± 0.002	1.30 ±0.001	4.51 ± 0.02	1.44± 0.01
leptin (ng/ml)	2.60-6.40	36.72 ± 0.15	4.69 ± 0.03	27.44 ± 0.45	5.52 ± 0.25
ghrelin (ng/ml)	0-100	76.05 ± 10.03	65.51 ±10.02	77.35 ±12.03	23.04 ± 0.01

Table 3. The logistic regression analysis shows correlation between TC, TG, LDL-C, VLDL-C and BMI, and the duration of the living in the North of MS group

	Regression coefficient	Standard error	Wald statistic Ch-square	P value	The achieved level of significance	Percentage of correct predictions
TC (mmol/L)	0.4389	0.0353	10.309	0.0111	0.0009	81.3
TG(mmol/L)	-0.0584	0.0097	8.7245	0.0740	0.0021	84.2
HDL-C(mmol/L)	-0.9504	0.0253	4.2382	0.0868	0.0326	86.1
LDL-C(mmol/L)	0.6589	0.0599	5.0256	0.1704	0.0191	87.3
VLDL- C(mmol/L)	0.1304	0.0777	0.1642	0.1700	0.0522	87.7
TG/HDL-C	1.1303	0.0114	0.3688	0.2915	0.0180	88.2

Table 4. Progression of obesity in patients with MS was associated with increased levels of serum leptin, ghrelin and leptin resistance (M±m)

BMI kg/m²	Leptin (ng/ml)	Ghrelin (ng/ml)	Leptin/ BMI
	Women		
The clinical group			
The normal weight (18.0-24.9)	4.00 ± 0.001	29.92 ± 2.35	0.5 ±0.01
The overweight (25.0-29.9)	8.09 ± 0.002	31.26 ± 3.65	0.77 ± 0.03
The obesity I (30.0-34.9)	16.20 ± 0.001	51.08 ± 11.44	0.81 ± 0.01
The obesity II (35.0-39.9)	40.70 ± 0.003	106.45 ± 15.25	1.10 ± 0.02
The obesity III (≤ 40)	78.90 ± 0.004	158.23 ± 12.25	1.62 ± 0.02
	Men		
The clinical group			
The normal weight (18.0-24.9)	3.02 ± 0.002	25.16 ± 1.36	0.2 ±0.01
The overweigth (25.0-29.9)	7.03 ± 0.001	29.32 ± 8.28	0.27 ± 0.01
The obesity I (30.0-34.9)	13.51 ± 0.001	31.05 ± 10.14	0.34 ± 0.02
The obesity II (35.0-39.9)	29.68 ± 0.002	76.24 ± 9.05	0.77 ± 0.01
The obesity III (≤ 40)	42.74 ± 0.002	169.15 ± 20.05	1.10 ± 0.01

Table 5 The logistic regression analysis shows correlation between TC, TG, LDL-C, VLDL-C and BMI, and testosterone and leptin of MS group

	Regression coefficient	Standard error	Wald statistic Ch-square	P value	The achieved level of significance	Percentage of correct predictions
	Woman					
TC (mmol/L)	0.5296	0.0134	12.458	0.0109	0.0004	80.1
TG(mmol/L)	0.3732	0.0076	9.3821	0.0580	0.0011	82.2
HDL-C(mmol/L)	-0.0098	0.0138	5.2567	0.0848	0.0016	92.1
LDL-C(mmol/L)	0.6156	0.0422	3.0221	0.1109	0.0009	83.4
VLDL- C(mmol/L)	0.0083	0.0568	0.1367	0.1240	0.0510	86.8
TG/HDL-C	0.7092	0.0092	0.3221	0.2104	0.0165	84.1
	Men					
TC (mmol/L)	0.1354	0.0205	12.211	0.0109	0.0002	91.1
TG(mmol/L)	-0.5100	0.0068	7.7109	0.0727	0.0017	85.3
HDL-C(mmol/L)	0.5109	0.0178	3.2034	0.0855	0.0271	87.2
LDL-C(mmol/L)	-0.4785	0.0462	1.0178	0.1609	0.0168	88.5
VLDL- C(mmol/L)	0.1221	0.0772	0.1523	0.1566	0.0477	88.1
TG/HDL-C	1.1206	0.0111	0.3011	0.2209	0.0109	82.6

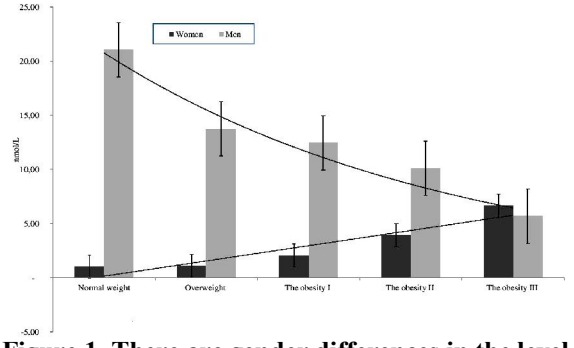

Figure 1. There are gender differences in the level of testosterone among men and women with an increase of obesity (p<0.001)

Figure 1 shows the gender differences in the level of serum testosterone, depending on obesity among men and women with MS.

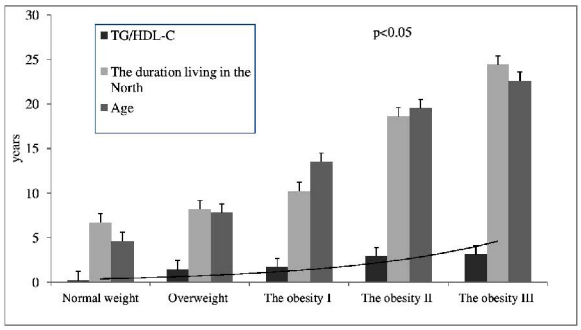

Figure 2. The risk of coronary heart disease is increased in patients of MS group longtime living in the North.

Figure 2 shows that risk of coronary heart disease is correlated with longtime living in the North and with the development of the obesity.

For the alien population of the northern regions is characterized the early manifestation and the rapid progression of the disease. By the process of the adaptation disorder influences as climatic, technological factors as the individual characteristics of the organism. The unfavorable influences of the climatic factors (low insolation, low temperature, change of the climate during the holidays) are increased by the negative influence of industrial factors [1]. The oil and gas industry makes up about 89.4% of all industries in the Khanty-Mansiysky autonomous district that it damages to the environment where a self-cleaning and a self-restoring are very slow [2].

The adaptation of people to the northern environment includes three phases: the destabilization (up to 2 years), the stabilization phase (2-4 years), the transition period (4-7 years) and the depletion phase (over 10 years) [5, 6]. Climatic and anthropogenic factors of the North lead to considerable energy and nutrients consumption of body. Indigenous people eat mainly the food with high amount of fat and proteins and with low amount of carbohydrates. The unsaturated fatty acid provides a high rate of lipids oxidation. This makes a favorable condition for the metabolism of lipids and defines the lower level of cholesterol [7, 10]. Many studies show that the metabolism of the indigenous population is higher than by the population of temperate latitudes. The result of two cross-studies of 320 inhabitants in the Republic Sakha showed the basal metabolism rate (8.5% men and 9.4% women) is higher than in the physiological standard [6].For the lipid metabolism of indigenous people is typical the increase of the lipoprotein lipase activity, the hepatic triglyceride lipase and HDL-C 60% that provide the process and the excretion of the fat from the body. At the «northern» type of the metabolism reduces the need of carbohydrates. It is known that the indigenous people of the North have a low level of glucose and insulin of the blood serum [8].

During the adapting of the alien population in the North is decreased the level of insulin and glucagon. However the catabolic processes do not prevails over the anabolic processes. The organism removes to a more economical type of the metabolic control using lipids. The oxidation of carbohydrates is decreased in tissues. Therefore for the energy ensuring of the body is used a free fatty acids, TG, LDL-C and VLDL-C [9].

The systematic abundance of carbohydrates in the diet can form obesity, diabetes and atherosclerosis. It is known that the alien population of the North eats more than a half of the carbohydrates at the expense of the refined sugars that promote to violations of cholesterol and fat metabolism [9].

The results showed that eating disorders were found among 60.5 % of all men and women, 86.6 % of these patients were clinical groups. In analyzing the results of styles of eating behavior among subjects clinical groups revealed differences in the styles between men and women. For women, the most typical type was emotiogenic behavior (41.0 %), which is reflected in the high dissatisfaction with the quality of life, in contrast to men, among which more type of externalities (50.6 %). During the follow-up observations 51.6 % of women and 46.1 % of men with metabolic syndrome tried to change your eating habits and save them for a longer period.

Emotiogenic and externalities food types in the diet contributed to the predominance of saturated fatty acids and carbohydrates, which reduces the rate of metabolism and contributes to obesity among residents of the North. Obesity of women has evolved in the first 10 years of life in the North. For men the degree of obesity has progressed with the duration of stay in the North. The increasing of the TC, TG, LDL-C level correlated with the growth of weight and BMI of men and women. However, we observed a decreasing HDL-C while the increasing BMI of MS women.

The progression of obesity among patients with MS correlated with increased levels of serum leptin. However, the normalizing of the level of leptin was achieved only among 5.3% of women and 8.5% of men. Leptin resistance was more common among women than among men. Indicator leptin / BMI of women with MS was higher at 36.4% than it was among men. So it remained a large number of fat

cells, we were not able to reduce the level of serum leptin. Propensity to leptin resistance and a higher content of leptin in the blood serum of women (32.1%) was than in men due to the lower inhibitory effect of estrogen on leptin than testosterone [10].

The amount of food consumed effects on the development of obesity. This contributes to the ghrelin-secreting cells of the stomach mainly. It is known that the concentration of ghrelin among healthy people after ingestion decreases. Among healthy control subjects, we observed no deviation ghrelin level in serum. The concentrations of ghrelin in the serum and blood glucose after meals decreased of normal and MS patients having obesity I degree. Many authors have noted decrease in the concentration of ghrelin at obesity and MS [11, 12].

It is believed that at lower levels of ghrelin gastric emptying rate does not decrease and a sense of satiety in obese persons does not arise. Therefore, obese people eat more than they need. This leads to hyperinflation and the stomach increases the density of receptors for ghrelin [13]. The results of our study confirm the increase in the concentration of ghrelin among obese patients with grade II and III. Ghrelin levels in serum were higher than the reference values of 16.2% among women, 22.9% among men. According to our information and researchers at the continuing high level of ghrelin in serum and diet-related patients with MS [14]. In the diet dominated by foods high in cholesterol and saturated fatty acids.

Significant influences of testosterone on dislipidemia, as the most active of all the hormones were differently among men and women. Sex differences have been identified in changes in lipid profile. Among the majority of women we observed an increase in triglyceride levels by 49.1 % and decreased HDL-C by 29.2 % compared with the control group, the men's total cholesterol level was higher by 27.9 %, LDL cholesterol by 23.4% compared with the control group. However, the observed significant differences were in the amount of lipoproteins. Since the level of total cholesterol in blood serum of men was 4.2% higher than among women with MS. Serum triglycerides of men with MS exceeded by 16.2 % ($P < 0.001$) the figure for women with MS.

This is because unlike estrogen increases the testosterone content of HDL, reduce - and LDL cholesterol, triglycerides and the level rises. There is a difference in the distribution of body fat (and women primarily in the subcutaneous fat layer) defines a higher level of leptin in the blood serum of women than it is among men. It is known that the synthesis of leptin is by adipocytes in the subcutaneous fat layer than it is in the visceral fat depot.

Reducing anti-atherogenic effect of estrogen and increased secretion of ovarian and adrenal androgens among 66.0% of patients with MS obesity contribute to the development of dislipidemia. MS patients were a trend towards reduction in serum testosterone (but within referent values) compared with healthy men. Obese patients activated aromatization of adrenal androgens to estrogens in adipocytes of visceral fat.

Conclusions

An important predictor of the risk of complications of 366 MS patients is the atherogenic dislipidemia. For MS patients is characterized the increase of TG, LDL-C and the decrease of HDL-C. These changes in the kinetics of metabolism of HDL-C are combined with the increase TG of VLDL, which indirectly leads to the decrease of HDL-C. The differences in dislipidemia depend on the influence of sex hormones among men and women, leptin, which is synthesized by adipocytes, and leptin resistance.

The long-time residence in the North, personality, the way of life defines principles of the keeping of health in the North. The changing of behavior leads to disturbing of adaption, to the increase of the cardiovascular risk, endocrine and metabolic diseases.

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Corresponding Author:
Dr.Korneeva Elena Victorovna
Surgut State University
Lenina Street, 1, Surgut, 628412, Russia

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