Vilnius University

Jelena Volochovič

# LONG-TERM RELATION BETWEEN ANTHROPOMETRIC AND METABOLIC CHANGES IN WOMEN WITH A RISK OF THE METABOLIC SYNDROME

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Doctoral dissertation was prepared at the Faculty of Medicine of Vilnius University in 2006 – 2010.

**Scientific tutors:**

Prof Dr Janina Didžiapetrienė (Institute of Oncology of Vilnius University, Biomedical Sciences, Medicine – 07 B) 2006-2007;

Prof Dr Gražina Drąsutienė (Clinic of Obstetrics-Gynaecology of the Faculty of Medicine of Vilnius University, Biomedical Sciences, Medicine – 07 B) 2007-2010 .

**Consultant:**

**Prof Dr Janina Tutkuvienė**, Department of Anatomy, Histology and Anthropology of the Faculty of Medicine of Vilnius University, Biomedical Sciences, Medicine – 07 B.

The dissertation is defended at the Board of the Medical Science Trend of Vilnius University:

**Chairman:**

Prof Habil Dr Aleksandras Laucevičius (Vilnius University, Biomedical Sciences, Medicine (07B)

**Members:**

Prof Habil Dr Vytautas Usonis (Vilnius University, Biomedical Sciences, Medicine (07B)

Prof Habil Dr Vaidutis Kučinskas (Vilnius University, Biomedical Sciences, Biology (01B)

Assoc Prof Dr Daiva Vaitkienė (Lithuanian University of Health Sciences, Biomedical Sciences, Medicine (07B)

Assoc Prof Dr Mykolas Mauricas (National Institute of Scientific Researches Centre of Innovative Medicine, Biomedical Sciences, Biology (01B)

**Oponents:**

Prof Dr Žaneta Petrulionienė (Vilnius University, Biomedical Sciences, Medicine (07B)

Prof Dr Dainius H. Pauža (Lithuanian University of Health Sciences, Biomedical Sciences, Biology (01B)

The dissertation will be defended at the meeting of the Board of the Medical Science Trend of Vilnius University on the 21st of December 2010, 14:00, at the Clinic of Obstetrics and Gynaecology of Vilnius University, Antakalnio str. 57, Vilnius.

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Vilniaus universitetas

Jelena Volochovič

# MOTERŲ ANTROPOMETRINIŲ IR MEDŽIAGŲ APYKAITOS RODIKLIŲ POKYČIŲ ILGALAIKIS RYŠYS SU METABOLINIO SINDROMO RIZIKA

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**Moksliniai vadovai:**

Prof. dr. Janina Didžiapetrienė (Vilniaus universiteto Onkologijos institutas, biomedicinos mokslai, medicina – 07B) 2006 – 2007 m. m.:

Prof. dr. Gražina Drąsutienė (Vilniaus universitetas, biomedicinos mokslai, medicina – 07B) 2007 – 2010 m. m.

**Konsultantas:**

Prof. dr. Janina Tutkuvienė (Vilniaus universitetas, biomedicinos mokslai, medicina – 07 B)

Disertacija ginama Vilniaus universiteto Medicinos mokslo krypties taryboje:

**Pirmininkas:**

Prof. habil. dr. Aleksandras Laucevičius (Vilniaus universitetas, biomedicinos mokslai, medicina– 07B).

**Nariai:**

Prof. habil. dr. Vytautas Usonis (Vilniaus universitetas, biomedicinos mokslai, medicina – 07B);

Prof. habil. dr. Vaidutis Kučinskas (Vilniaus universitetas, biomedicinos mokslai, biologija – 01B);

Doc. dr. Daiva Vaitkienė (Lietuvos sveikatos mokslų universitetas, biomedicinos mokslai, medicina– 07B);

Doc. dr. Mykolas Mauricas (Valstybinio mokslinio tyrimų instituto Inovatyvios medicinos centras, biomedicinos mokslai, biologija – 01B)

**Oponentai:**

Prof. dr. Žaneta Petrulionienė (Vilniaus universitetas, biomedicinos mokslai, medicina – 07B);

Prof. dr. Dainius Haroldas Pauža (Lietuvos sveikatos mokslų universitetas, biomedicinos mokslai, biologija – 01B).

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## MOSTLY USED CONCEPTS AND ABBREVIATIONS

AC – Atherogenic Coefficient

ABP – arterial blood pressure

AHA 2009 – A Joint Interim Statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity recommended criteria of diagnostics of the metabolic syndrome

AHA/NHLBI – American Heart Association / National Heart, Lung, and Blood Institute

AIP –Atherogenic Index of Plasma

BMI – body mass index

Ch – cholesterol

CHD – coronary heart disease

CI - confidence interval

DM – diabetes mellitus

GDM – gestational diabetes mellitus

HDL – high-density lipoprotein

IDF 2005– The International Diabetes Federation recommended criteria of diagnostics of the metabolic syndrome

IUGR - intrauterine growth restriction

LDL – low-density lipoprotein

LPL – lipoprotein lipase

M – mean

Max – maximal value

Min – minimal value

MS – metabolic syndrome

NCEP/ATP III 2001– Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults /Adult Treatment Panel III recommended criteria of diagnostics of the metabolic syndrome

Non-HDL – non-high-density lipoprotein

OGTT – oral glucose tolerance test

OR – odds ratio

p – level of significance

PCOS - polycystic ovary syndrome

PPAR-γ – peroxisome proliferator-activated receptor

*r* – correlation coefficient

SD – standard deviation

Tg – triacylglicerols

VLDL – very low densty lipoprotein

WHO 1998– The World Health Organization recommended criteria of diagnostics of the metabolic syndrome

WHR – waist-to-hip ratio

$\chi^2$ – criterion of chi square

# 1. INTRODUCTION

## 1.1. Problem

Last decades were the years of conception of significant economic, social and moral values in Lithuania. Demographic rates in our country have reached the critic line.

Over the last five years the negative change of population has been observed in Lithuania: from -1,6 (in 2009) to -4,0 (in 2006). Even the increased number of births (in 2007 – 29141, in 2008 – 31052, in 2009 – 32145 births) didn‘t have positive impact on the rate of natural change of population [1].

Unabated emigration (in 2007 4,1/1000 people left Lithuania, in 2009 – 6,6/1000 people) even worsens the demographic situation of the country [2].

Lithuanian demographic situation and negative changes of natural increase bind over a medical community to provide qualified aid to women in every period of life when focusing on the reproductive health. A newborn‘s as well as future generation‘s health and thus the health of Lithuanian society in the future depend on the woman health. Rates of mother and child health are a prenatal mortality of pregnant women, newborns and babies as well as women morbidity reflect the social and economical development of the country.

In accordance with the data of the Department of Statistics under the Government of the Republic of Lithuania in 2008-2010 women made up 53,5 percent of all Lithuanian population, men - 46,5 percent [3].

In 2008 the average lifespan was 77,6 years, in 2009 – 78,6 years, respectively men lived for 66,3 and 67,5 years [4]. Therefore, female lifespan exceeds men lifespan for ten years. However, this difference of possible lifespan between men and women is not directly related with the quality and health of women life.

The number of overweighed or obese women is increasing; there are more and more diseases caused by body weight and excess of adipose tissue – cardiovascular diseases, DM, metabolic syndrome [5–9].

The growing number of diseases related to obesity has serious economic consequences. It was calculated that 7 percent of health care costs are allocated to the treatment of obesity in the European Union, meanwhile the medical costs of an adult in USA are higher for 37 percent than average body weight [10].

The periods of woman lifespan are accompanied by anthropometric, physical changes of various metabolic links, which often balance with the pathology. Therefore, the task for obstetrician gynecologist is to evaluate them, identify risk groups and diagnose the disease on time.

Pregnancy is a period of time when a woman is in a constant medical care. Therefore, the care of pregnancy to the health care professional is a real opportunity to observe the physical changes of a pregnant woman, to perform clinical laboratory tests, evaluate the risk of individual even more remote diseases and start applying preventive measures early.

### 1.2 Relevance and scientific newness of work

There are traditions of researching the anthropometric and metabolic peculiarities in women at the Clinic of Obstetrics and Gynaecology of Vilnius University [11, 12]. This scientific research is a part and follow-up of these works.

This work is the first long-term linear research of this type in Lithuania which aim is to determine the tendencies of body mass and metabolic changes in women related with their age. Our research is the longest known research of observing the body structure and metabolic changes in women during pregnancy and after it. Up to now, researches of that type performed abroad have lasted for 15 years [13–15]. In the performed work, the relations of a long-term risk of MS with the body composition and metabolic changes in women had happened during their previous pregnancies have been assessed for the first time in Lithuania. Besides, the research assessed the relation of the adipokines profile parameters with physiological and pathological conditions in women.

### 1.3 Theoretic and applicable meaning of work

The results of the work provide new information about the body composition and metabolic changes in women related with their age and reveal unfavourable tendencies of these changes. The results of the work can help to early and more exactly determine the groups of women with an increased risk of the MS development make the research plan and take measures of the primary prophylaxis earlier. A few body markers are suggested which can indicate an increased risk of the MS development.

The data accumulated by us can become reason for the follow-up in this field.

## 2. AIM OF WORK

To assess the changes in the anthropometric and metabolic parameters in women within twenty years and long-term relation of these changes with a risk of the metabolic syndrome.

## 3. TASKS OF WORK

1. To assess the changes in the body mass, BMI and adipose tissue accumulation in the researched women within twenty years.
2. To assess the changes in the lipid and carbohydrate metabolism parameters in the researched women within twenty years.
3. To assess the peculiarities of the adipose tissue accumulation in the researched healthy or metabolic syndrome women during pregnancy and in twenty years after giving birth.
4. To assess the peculiarities of the lipid and carbohydrate metabolism parameters in the researched healthy or metabolic syndrome women during pregnancy and in twenty years after giving birth.
5. To assess the adipokines metabolism parameters in the researched women and their relation with physiological and pathological conditions in women.

## 4. DEFENDED PROPOSITIONS

1. With the increasing age a female body faces negative anthropometric and metabolic changes of various links.
2. For women with a predisposition to metabolic syndrome, during pregnancy can already be detected early anthropometric indicators.

## 5. REVIEW OF LITERATURE

220 literary sources have been chosen for the review of literature and interpretation of the results of the researches.

### 5.1 Adipose tissue – its topography and meaning for the function and pathology of the women's reproductive system

The adipose tissue is a body organ situated in the total organism [16]. It has been determined an increase in the amount of the adipose tissue within the first year of life depends on an increase in the volume of fatty cells and within the period of maturation – on an increase in the amount of fatty cells themselves [17].

About 65–70 percent of the adipose tissue falls to the subcutaneous adipose layer, 30–35 percent – to the visceral adipose tissue [16]. According to the histological structure, the white and brown adipose tissue is classified [16, 18].

Constant regeneration is characteristic to the adipose tissue; this process is regulated by a complicated interaction among genes, cytokines, hormone system and environmental factors [16, 19]. Adipogenesis is stimulated by: Early growth response or Krox factors, PRAR-γ agonists, Krupel-like factor 5, 6, 7, 15 [19–21]. Adipogenesis is inhibited by: transcription factors GATA-2, GATA-3, Foxo1 and 2, Krupel-like factor 2, SMAD-3, WNT-10b [19, 21]. Mature adipocytes are defined by the following markers: PRAR-γ, LPL, adipokines [19].

For a long time, the adipose tissue was understood as a place of accumulation of energetic materials in the organism, a protective layer of the body and internal organs, a part of the thermoregulation system of the organism. In 1953 Kennedy made a hypothesis the adipose tissue both accumulated energetic materials and performed the function of the endocrine gland [22]. In 1987 the results of the researches were announced which proved the meaning of the adipose tissue in the sexual hormone metabolism [23]. In 1994 the first biologically active factor excreted by the adipose tissue – leptin – was described [24]. On the basis of the present knowledge, it is possible to state the adipose tissue is characterized with the properties of an endocrine organ and the materials produced by it – with the autocrine, paracrine and endocrine impact [25, 26, 43].

It is indicated in the literature the composition of the adipose tissue of different localization and its impact on the organism is different due to different metabolism [16, 31–33].

### 5.2 Adiposopathy

Harold E. Bays suggested the term adiposopathy [33, 36–42]. This is a definition of the dysfunction of the adipose tissue which develops as a secondary phenomenon in case a person has an excess of the adipose tissue, his/her physical activity is not sufficient and he/she has a genetic tendency to disorders of the function of the adipose tissue.

In case of constant positive diet calorage, there are disorders of adipogenesis and distribution of the adipose tissue in the organism, function of the adipose tissue as of an endocrine organ and a part of the immune system of the organism and interaction of the adipose tissue with the other organs and organ systems. These processes stimulate excessive fat-related metabolic diseases.

### 5.3 Adipokines

Adipokines are biologically active materials related with the adipose tissue. They act in the organism by using their central and peripheral receptors. Adipokines and receptors ensure for adipokines the interaction of the adipose tissue with the other systems in the organism – nervous, immune and endocrine gland systems.

**Leptin** was first described in 1994 [24]. Human leptin which consists of 167 amino acids is a product of *Ob* gene. Human *Ob* gene is in the $7^{th}$ chromosome (7q32) [44]. The molecular mass of leptin is 18 kDa, but leptin of 16 kDa only gets to bloodstream after the removal of the signal fragment [45]. Most leptin is produced by the adipose tissue, but placenta, stomach, brain, muscles and fibroblasts can also produce and excrete leptin *in vitro* and *in situ* [35, 46]. The production of leptin is stimulated by the consumption of food, glucocorticoids, estrogens, insulin, TNF-$\alpha$ and IL-1. The expression of *Ob* gene is decreased by androgens, growth hormone, stimulation of the sympathetic nervous system (low temperature, noradrenalin) and long-lasting starvation. Most receptors of leptin *Ob-R* are contained in the central nervous system. There also are receptors of leptin in the adipose tissue itself, lungs, kidneys, thyroid, gonads, placenta, muscles, endothelium, β cells of pancreas and T lymphocytes. The signal of leptin is

transmitted in a few ways: through JAK-STAT system (*Janus kinases-signal transducers and activators of transcription*), cascade MAPK (*mitogen-activated protein kinase*) and AMPK (*AMP-activated protein kinase*) activation [47]. Leptin is characterized by lipostatic properties, decreases the production of neuropeptide Y, agouti-related peptide and other orexogenic neuropeptides and increases the concentration of anorexogenic mediators. Leptin decreases the production of insulin and transmission of glucoses to adipocytes, Tg and fatty acid synthesis, increases the oxidation of fatty acids and decreases the accumulation of lipids in cells. It impacts the function of endocrine glands, function of the cardiovascular system, regulates the arterial blood pressure and positively impacts angiogenesis. Leptin activates macrophages and monocytes, regulates phagocytosis, causes the proliferation of naive T cells and inhibits the proliferation of T memory cells. In the periphery it regulates the metabolism of blood formation, pancreas, muscle cells and hepatocyte materials containing *Ob-R* receptors [35].

**Adiponectin** was first described in 1999 [48, 49]. Adiponectin is a polypeptide which molecular mass is 33 kDa [35]. The gene of adiponectin is in the 3$^{rd}$ chromosome (3q27). The main source of adiponectin in the organism is adipocytes. It is both possible to detect the general adiponectin concentration and its fractions in serum *(HMW – high-molecular-weight, MMW – medium-molecular-weight, LMW – low-molecular-weight)* [50, 51]. The adiponectin synthesis and excretion is stimulated by insulin, PPAR-γ agonists and decrease in the body mass; it is inhibited by PPAR-γ antagonists, TNF-α and obesity. Adiponectin is detected in higher concentration in the subcutaneous adipose tissue than in the visceral one. In serum the adiponectin and HDL cholesterol concentrations correlate positively and the correlation among the adiponectin concentration and arterial blood pressure, glycaemia without eating, insulin, Tg and LDL cholesterol concentrations is negative. Adiponectin is characterized by an anti-diabetes, inflammation-inhibitive and vessel-protective impact [34, 35, 49].

In the literature other adipokines are described in a comprehensive way – these are resistin [35, 52], visfatin [53–55], omentin [56, 57] and apelin [58, 59]. Lately, there have been some publications about new adipokines – adrenomedulin, chemenin, ghrelin, *Complement-C1q TNF-related protein 1* and *Retinol-binding protein 4* [60–64].

Fluctuations in the expression of adipokines in the organism tissues and serum concentration indexes are related with the body mass, resistance to insulin and MS,

osteoporosis, arterial hypertension and hematological diseases. The peculiarities of the impact of adipokines on the woman's organism during the period of maturation, in case of infertility (especially PCOS), pathology of the endometrium, physiological pregnancy and lactation and pathology of pregnancy are researched. A special attention by the researchers is paid to the pathology of pregnancy – preeclampsia, GDM and DM, IUGR and macrosomia. Changes in the expression of adipokines in the tissues and serum concentration in case of physiological and pathological conditions are presented in tables 1 and 2 [50, 51, 65, 66, 69–83, 87– 105, 219].

In the scientific literature both changes in the concentrations of separate adipokines are analyzed and leptin/adiponectin and adiponectin/leptin and adiponectin/BMI ratios are assessed [106–112].

**Table 1**: Expression of adipokines in the tissues and serum concentration in case of physiological and pathological conditions

| Groups of persons or conditions | Leptin | Adiponectin | Resistin |
|---|---|---|---|
| Women *versus* men | ↑* [66, 100] | ↑ [66, 87, 100] | ↑ar ↓ [66] |
| City *versus* country dwellers | | ↓ [87] | |
| White race | | ↑ [88] | |
| Maturation | ↑ [66] | ↑ar ↓ [66] | ↑ [66] |
| Follicle phase | ↓ [90] | | |
| Luteal phase | ↑ [90] | ↓ ar = [70, 91, 92] | |
| Pregnancy | ↑ (iki III nėštumo trimestro), ↓ (artėjant gimdymui) [65, 69] | ↓ ar ↑ (kai KMI normalus), ↑HMW, ↓LMW ir =MMW [51, 70] | ↑ [71] |
| After birth | ↓ (iki buvusio prieš nėštumą lygio per 24 val.) [69] | ↓ [72] | ↓ [73, 74] |
| Perimenopause | ↑ (normalus KMI) ar = (nutukusios) [93, 94] | ↓ ar = [93, 94] | ↓ [93] |
| Postmenopause | | ↑ [94] | |

*) Tables 1 and 2: ↑ – Expression or concentration increases, ↓ – decreases, = – does not change.

**Table 2**: Expression of adipokines in the tissues and serum concentration in case of diseases and pathological conditions

| Diseases or pathological conditions | Leptin | Adiponectin | Resistin |
|---|---|---|---|
| Obesity | ↑* [66, 101] | ↓ ar<br>↑ [66, 102–104] | ↑ ar = [66] |
| *Anorexia nervosa* | ↓ [105] | ↑ [105] | = [105] |
| Atherosclerosis | ↑ [101] | ↑ [101] | ↑ [101] |
| Resistance to insulin | ↑ [102] | ↓ [67, 102] | = [106] |
| Coronary heart disease | | ↓ [89] | |
| MS | | ↓ [219] | |
| Weight reduction | ↓ [66] | ↑ ar ↓ [66] | |
| PCOS | ↑ [66] | = ar ↓ [66–68] | ↑ [66] |
| Preeclampsia | ↑ [75, 85] | ↑ ar = ar ↓,<br>↓HMW, ↑MMW<br>[75–77, 85] | ↓ ar ↑ ar =<br>[85, 96] |
| GDM | ↑ar ↓ ar = (greičiausiai priklauso nuo glikemijos kontrolės) [78, 84] | ↓, ↓HMW, ↑MMW<br>[79–81] | ↑ar ↓ [73, 74, 79] |
| Premature birth | | ↓, ↓HMW, ↑LMW<br>[97] | |
| Macrosomia | ↑ [65, 82] | ↓ [82] | ↓ [82] |
| IUGR | ↓ [83] | ↑ ar ↓, ↓HMW,<br>↑MMW [50, 83] | |
| Alcohol consumption** | ↑ [98] | ↑[98] | ↓ ar ↑ [98, 99] |

**) Determined after performing experiments with animals.

## 5.4 Changes in the women's body composition

### *5.4.1 Changes in the anthropometric parameters in women during pregnancy*

According to the data by various authors, in the period of pregnancy the total amount of the adipose tissue in a woman increases by 3,5–4,6 kg [12, 114, 115]. According to the data by Lithuanian authors, during pregnancy the woman's body mass increases by 13,3–14,2 kg on the average [11, 116]. The authors of linear researches performed in Great Britain and Sweden indicate an augment in the body mass in

pregnant women is 10,9-16,3 kg [13, 114]. An augment in the body mass during pregnancy is a physiological phenomenon; however, there are its physiological limits. They largely depend on the woman's BMI before pregnancy [115, 117].

The body mass and BMI indicators in women after birth often remain higher than they were before pregnancy. *SPAWN* research indicated an augment in the body mass in women was 0,5-3,7 kg within 2,5 years when calculating from early pregnancy, and within 15 years after birth the body mass increased by 6,2 kg on the average [13, 15]. Even 73 percent women surveyed during *SPAWN* research indicated pregnancy was the reason for a remaining augment in the body mass [13].

There is little data about long-term changes in the body mass after previous pregnancies and births in the literature. Both the data of short-lasting (up to 6 months) researches and that of long-term observations (up to 15 years) shows women who weighted more kilos during pregnancy risked having a bigger body mass and BMI in the future [13, 14, 114, 118]. Researches proved BMI of a distant period correlated with BMI before pregnancy, augment in the body mass during pregnancy and loss in the body mass within 6 months after birth [120]. Other authors state they have not detected any bigger differences between the body mass and BMI indicators after pregnancy and birth according to BMI before pregnancy [119].

### *5.4.2 Changes in the anthropometric parameters in women during perimenopause*

According to the literary data, the body mass in women during perimenopause can increase by about 0,5 kg per year [121]. By applying DEXA, MRI, CT methods, scientists of the USA have proved the centralization of the adipose tissue occurred in the period of perimenopause [122–126]. It has been proved the total fatty tissue mass increases in the women's organism after menopause by 28 percent compared with that before menopause, the subcutaneous adipose tissue mass increases by 36 percent, the subcutaneous adipose tissue mass in the abdominal region – by 22 percent and the visceral adipose tissue mass – by even 49 percent [122–124]. Canadian scientists pay attention to "fattening" internal organs and muscles beside the changes above [127].

Lithuanian authors determined a negative meaning of obesity for social factors – women's life quality, satisfaction with their appearance and psychological state of independence [8]. Thus, unfavourable metabolic changes in the body structure happen in middle-aged women's organism, especially after menopause.

The reasons for an augment in the body mass, obesity and centralization of the adipose tissue during perimenopause are related with the metabolism slowdown, remaining bad nutritional habits, insufficient physical activity and development of resistance to insulin [121, 126, 128]. Other reasons can also be distinguished: changes in the growth hormone, leptin, galanin, ghrelin and neuropeptide Y concentrations [130, 131]. Some authors indicate the changes caused by the factor of infection (for example, adenovirus Ad-36) as a possible reason for obesity [132, 133].

## 5.5 Metabolic changes in women in different periods of life

### *5.5.1 Metabolic peculiarities in pregnant women*

Metabolism physiologically changes during pregnancy. It has been calculated the total "energy expenditures" of the organism which are related with pregnancy reach up to 80 000 kcal and only about 10 000 kcal are "absorbed" [140].

**Lipid metabolism.** According to the data by Lithuanian authors, both Ch and Tg concentrations significantly increase during pregnancy and in late pregnancy are higher than the upper threshold set for non-pregnant women [11, 12, 116]. The lipid metabolism indexes and BMI during pregnancy are reversely correlated – the higher is BMI in early pregnancy, the less increases the lipid concentration during pregnancy [139, 141, 142]. According to the literary data, the total Ch concentration decreases a little during the first pregnancy trimester, largely increases during the second one and decreases a little during the third one, but it remains higher compared with the values before pregnancy. Within a year after birth, the total Ch concentration coincides with that before pregnancy. Tendencies in the changes in the LDL cholesterol and Tg concentrations coincide with the changes in the total Ch concentration above. The HDL cholesterol concentration does not change during the first pregnancy trimester, largely increases during the second one and decreases during the third one. Within a year after birth, the HDL cholesterol concentration never reaches its level before pregnancy. A few consecutive pregnancies are characterized by the cumulative impact on a decrease in the HDL cholesterol concentration. AIP also increases during the third pregnancy trimester [139, 141].

In case pregnancy is complicated, the changes in the lipid metabolism can be even more dramatic [143–146]. In the literature a possible relation among dyslipidaemia,

GDM, premature birth, infective and inflammatory processes and IUGR is analyzed [144, 147-151].

**Carbohydrate metabolism.** In order to ensure the needs of the foetus' growth and development, the production of glucose in the pregnant woman's organism increases from 16 to 30 percent [150]. In order to ensure a normal glucose concentration for the pregnant woman, the production of insulin significantly increases and the insulin and glucose concentrations are reversely correlated [150, 152]. Due to increased production of glucose, growth factors excreted during pregnancy and fatty tissue accumulation, a relative resistance to insulin develops in the pregnant woman's organism and it correlates with the amount of the fatty tissue in the pregnant woman [152, 153].

In case of complicated pregnancy, these changes are more dramatic [154, 155]. Italian scientists have determined MS components are found within 6-8 years in those women who had hyperglycaemia during pregnancy 2-4 times more frequently compared with those whose glucose concentration was normal in the period of pregnancy. Besides, a risk of developing MS increases by even 10 times if the pregnant woman with hyperglycaemia was obese before pregnancy [156, 157]. Canadian scientists have found an increased resistance to insulin among the women whose OGTT results were pathological [158].

### *5.5.2 Metabolism peculiarities during perimenopause*

As the woman is ageing, the lipid concentrations in her organism obtain a characteristic proatherogenic profile – there is a statistic-significant increase in the Ch, Tg and LDL cholesterol concentrations and a decrease in the HDL cholesterol concentration [159–161]. The lipid concentrations reach atherogenic values and the ratio between the Tg and HDL cholesterol concentrations significantly increases [162]. According to the data by scientists of the USA, the changes in the lipid concentrations positively correlate with the changes in the insulin concentration (HDL cholesterol and insulin parameters, Tg and insulin parameters) and sexual hormone concentration (HDL cholesterol and free testosterone indexes) [160, 161]. Dyslipidaemia is also related with a decrease in the activity of LPL [163].

The data of *Chin-Shan Community Cohort study* have indicated the changes in the Tg, total Ch, LDL cholesterol concentrations also correlate with women's age and the changes in the Tg, LDL cholesterol and HDL cholesterol concentrations also correlate

with BMI [164]. The authors of *Fels Longitudinal Study* have determined an analogical relation between the Tg concentration and age and confirmed the relation between an increase in the amount of the adipose tissue and an increase in the total Ch, Tg and LDL cholesterol concentrations [161]. Researches of scientists of the USA and Asia have shown menopause itself is an independent risk factor of hyperglycaemia and resistance to insulin independently from age, BMI, Tg and LDL cholesterol concentrations [165–167]. It has been determined even 16 percent women after menopause are resistant to insulin [167]. On the other hand, the time of menopause depends on the present metabolic disorders. Scientists of the USA have determined menopause manifests for ill women with DM of type I by 7–9 earlier than for healthy ones [168].

Proatherogenic metabolic changes related with women's age and menopause correlated with anthropometric changes in the distribution of the adipose tissue. A positive correlative relation between the resistance to insulin and WHR and relation between the changes in the total Ch and LDL cholesterol concentrations and an increase in the visceral fatty tissue has been found [169].

Thus, the following metabolic changes develop in women after menopause – dyslipidaemia, resistance to insulin and hyperglycaemia. They make components of MS and increase a risk of cardiovascular diseases. Therefore, recommendations for the lipid profile control for women after menopause have been set [170]. It is recommended to determine the risk degree by using *SCORE* risk scale [171].

### 5.6 Metabolic syndrome

The metabolic syndrome (MS) is the whole of clinical and biochemical changes caused by resistance to insulin. We can find other names of this syndrome in the scientific literature: polymetabolic syndrome, plurimetabolic syndrome, dysmetabolic syndrome, X syndrome, chaos syndrome, deadly quartet, insulin-resistance syndrome [172]. In 1967 in the first congress of the *European Association for the Study of Diabetes* Pietro Avogaro gave the name of the plurimetabolic syndrome to the coexistence of abdominal obesity, hypertension and lipid and carbohydrate disorders and discussed the meaning of this syndrome to a risk of the CHD [173]. In 1988 Gerald M. Reaven paid attention to the role of resistance to insulin in the etiology of atherosclerosis [174]. A year later, Norman M. Kaplan picturesquely described a so-called *deadly quartet* –

central obesity, arterial hypertension, glucose-tolerance disorder and hypertriacylglycerolaemia [175].

The list of components of MS increased as there were more and more scientific researches performed in respect of this topic [172, 176–201]. According to the data by Lithuanian authors, components of MS manifested in the group of patients with the CHD especially frequently: arterial hypertension in 36,2–55,3 percent, DM – in 9,7–23,4 and dyslipidaemia – even in 88,9–97,6 percent of these patients [6].

Finally, *WHO* recommended to use one name of MS and suggested the criteria of diagnosing this syndrome [176]. Later other diagnostic and stricter methods were developed and recommended [177, 178, 202, 203]. The latest recommendations were generalized and published in 2009 - AHA criteria of diagnosing the MS [203].

According to the data by various authors, when considering the methodology used for diagnosing MS, the rate of this syndrome in the asymptomatic population is 22–35 percent and among those with DM – even 65 percent. The rate of MS increases when ageing. MS is diagnosed in men more frequently [204, 205]. According to the data by Lithuanian authors, the rate of MS among men is 11,3–34,4 percent and among women – 9,4–54,1 percent. The data about proportions among the sexes are contradictory [5, 7, 206, 207].

Ethiopatogenesis of MS has not been researched to the utmost, but most authors agree metabolic disorders are caused by resistance to insulin [35, 143, 175]. It is supposed the development of resistance to insulin may be both influenced by congenital and acquired factors [172]. There is some data MS can develop not only in overweighed or obese people, but also in people with normal BMI [209].

A lot of disorders in the obstetrician-gynaecologists' range are related with MS. These disorders include PCOS, infertility and problems of its treatment (danger of OHSS), dysfunctional bleeding and conditions related with relative hyperestremia – hyperplasia of the uterus mucous membrane and risk of cancer, pathology of pregnancy – GDM, preeclampsia, preterm birth, IUGR and macrosomia [179, 190–195, 197–199, 200, 211, 212].

# 6. RESEARCH MATERIAL AND METHODS

## 6.1 Research material

This work is the follow-up of the scientific project started by the Clinic of Obstetrics and Gynaecology of Vilnius University in 1986-1987.

At the beginning of the researched period, i.e., in 1986-1987 (hereinafter – first research), 386 healthy pregnant women were researched. The women were selected for the research in the way of a random selection in their early pregnancy. The data of the researches performed during early and late pregnancy was used for this work.

At the end of the research, i.e., in 2006-2008 (hereinafter – second research), we succeeded in contacting with 108 women or their family members from 386 participants of the first research (28 percent). 26 of 108 women refused to participate in the research, 21 women had left Lithuania and one participant of the previous research had died. Only 60 participants of the previous research (15,5 percent) arrived for the follow-up.

## 6.2 Research methods

### *6.2.1 Questionnaire survey*

The data about the women's diseases was collected during the first and second research of the obstetric and gynaecologic anamnesis by using the method of a questionnaire survey.

### *6.2.2 Anthropometric parameters*

For all the women, the following anthropometric measurements were performed in early pregnancy, late pregnancy and within 20 years and the anthropometric parameters were calculated:

The **height** was measured with a standard vertical height meter (measurement accuracy ± 5 mm) by following the usual requirements for the body position.

During the first research, the **body mass** was measured with a medical Ferbenks scale which accuracy is 100 g. During the second research, the woman's body mass was measured with a medical electronic scale which accuracy is 100 g. The researched women were weighed in the morning without eating, with light clothes and after urinating.

**BMI** was calculated according to the following formula:

$$BMI = \text{body mass (kg)} / \text{height (m)}^2.$$

The **body circumferences** were measured with a centimetre strip which was periodically changed. For the researched women, the chest and waist circumferences were determined and the hip circumference was also added during the second research.

The **waist-hip ratio** (WHR) was calculated according to the following formula:

$$WHR = \text{waist circumference (cm)} / \text{hip circumference (cm)}.$$

The **thickness of skin folds** was measured on the right side of the body with a Holtain-type calliper (*Siber Hegner*, Swiss), scale 400 mm, step 0,2 mm and fold squeeze pressure 10 g/mm$^2$. The same fold was measured three times and the arithmetic mean was calculated and recorded. Eight skin folds were measured according to a special measurement methodology [213]: chin, chest, subscapular, biceps, triceps, abdomen, femoral and calf.

The following **amounts of skin folds** were calculated:

- The amount of eight skin folds was calculated by summing up the readings of chin, chest, subscapular, biceps, triceps, abdomen, femoral and calf skin folds;
- The amount of skin folds of the upper part of the body was calculated by summing up the readings of chin, chest, subscapular, biceps and triceps skin folds;
- The amount of skin folds of the lower part of the body was calculated by summing up the readings of abdomen, femoral and calf skin folds;
- The amount of torsio skin folds was calculated by summing up the readings of chin, chest, subscapular and abdomen skin folds;
- The amount of skin folds of the upper part of the torsio was calculated by summing up the readings of chin, chest and subscapular skin folds;
- The amount of limb skin folds was calculated by summing up the readings of biceps and triceps, femoral and calf skin folds;
- The amount of skin folds of the upper limb was calculated by summing up the readings of biceps and triceps skin folds;
- The amount of skin folds of the lower limb was calculated by summing up the readings of femoral and calf skin folds.

The following ratios of the **amounts of skin folds** were calculated:

Ratio between the amount of skin folds of the upper part of the body and the amount of skin folds of the lower part of the body;

Ratio between the amount of torsio skin folds and the amount of limb skin folds;

Ratio between the amount of skin holds of the upper part of the torsio and the amount of eight skin folds.

The **relative passive body mass** was calculated according to the following formulas:

1. Body thickness (BT) – according to Wilmore-Behnke's formula [214]:

$$BT = 1{,}06234 – 0{,}00068(X1) – 0{,}00039(X2) – 0{,}00025(X3),$$

Where: X1 – subscapular, X2 – humeral posterior, X3 – femoral skin fold.

2. Rate of the passive body mass – according to Siri's formula [215]:

$$[(4{,}95 / CT) – 4{,}50] \times 100.$$

The **absolute amount of the passive body mass** was calculated according to the following formula:

$$(\text{Body mass} \times \text{passive mass per cent}) / 100.$$

**Fat mass Ratio** was calculated according to the following formula:

$$\text{Passive mass (kg)} / \text{height (m)}^2.$$

The **neonates' body mass** was immediately assessed after birth. The neonates were weighed with an electronic scale for neonates which accuracy is 20 g. The neonates' sex was recorded. *Note.* When assessing the data of the neonates' birth mass, we excluded the twins' parameters.

The **ratio between an augment in the passive body mass during pregnancy (kg) and the neonate's birth mass (kg)** was calculated.

### *6.2.3 Metabolic parameters*

Blood for examinations was collected from the elbow of the women who had not eaten for more than 12 hours and it was directly added to vacuum tubes. The examinations were performed at the Laboratory Diagnostics Centre of Vilnius University Hospital "Santariškių klinikos".

#### *6.2.3.1 Lipid metabolism parameters*

In 1986-1987 the **total cholesterol, HDL cholesterol, LDL cholesterol and triacylglicerols concentrations** in serum were determined by using *Lachema* reagents (Czech) [12]. In 2006-2008 the total Ch, HDL cholesterol, LDL cholesterol and Tg concentrations were examined with the biochemical analyzer *Dimension RxL (Siemens)* by using *Dade Behring Inc.* Reagents (USA).

The following derived lipid metabolism parameters were calculated:

The **very-low-density lipoprotein cholesterol concentration** (VLDL cholesterol) in serum was calculated according to the following formula [108]:

VLDL cholesterol = Ch – HDL cholesterol – LDL cholesterol.

The **non-high density lipoprotein cholesterol concentration** (non-HDL cholesterol) in serum was calculated according to the following formula:

non-HDL cholesterol = Ch – DTL.

The **atherogenic coefficient** (AC) was calculated according to the following formula [184]:

AC = (Ch – HDL cholesterol)/ HDL cholesterol.

The **atherogenic index of plasma** (AIP) was calculated according to the following formula [110]:

AIP = log (Tg/HDL cholesterol – Ch).

The following **ratios between the lipid metabolism indexes** were calculated: (LDL cholesterol/HDL cholesterol), (Ch/HDL cholesterol) and (Tg/HDL cholesterol).

#### *6.2.3.2 Carbohydrate metabolism parameters*

During the first research, the **glucose concentration** in serum was determined with the analyzer *Eksan-G* (Lithuania) by using the glucosoxidative method [12]. During the second research, the **glucose concentration** was determined with the biochemical analyzer *Dimension RxL (Siemens)* by using *Dade Behring Inc.* Reagents (USA).

The **insulin concentration** in serum was determined with the analyzer *IMMULITE 2000 (Siemens)* by using the method of the solid phase double chemiluminescent immunometric analysis.

The **resistance to insulin** was determined by using HOMA-IR index according to the following formula [217]:

HOMA-IR =

(Insulin without eating [mU/ml]) × (glucose without eating [mmol/l]) / 22,5.

### *6.2.3.3 Adipokines metabolism parameters*

The **leptin concentration** in serum was determined in the immunoradiometric method and by using *Human Leptin IRMA DSL-23100i (Diagnostic Systems Laboratories Inc., USA)* reagents.

The **adiponectin concentration** in serum was determined in the radioimmune method and by using *Human Adiponectin RIA Kit* (*LINCO Research, USA*) reagents. The values of the norm of the adiponectin concentration in serum are not indicated and the assessment is individual.

The following **relative indexes of the adiponectin metabolism** were calculated:

- Ratio between the leptin concentration and the adiponectin concentration (hereinafter – leptin/adiponectin);
- The ratio of the adiponectin concentration and women's BMI (hereinafter – adiponectin/BMI).

### *6.2.4 Clinical researches*

For the researched women, the **arterial blood pressure** was measured according to AHA recommendations [218] with a mercury sphygmomanometer, after the women had relaxed and in a comfortable sitting position. The arterial blood pressure was measured on the both arms three times and the mean of the received data was recorded.

### *6.2.5 Criteria of diagnostics of metabolic syndrome*

According to the research results of 2006–2008, the **metabolic syndrome** was found in the women (hereinafter – MS). The women were divided into two groups – MS (+), i.e., with the metabolic syndrome (22 women) and MS (-), i.e., healthy women (38 women).

The diagnosis of MS was determined in the researched by applying the diagnostic criteria of AHA 2009 [202]. MS was determined for the women whose measured

abdominal circumference was > 80 cm and at least two of the following criteria were found:

Increased Tg concentration ≥ 1,7 mmol/l or used drugs for dyslipidaemia;

Decreased HDL cholesterol concentration < 1,3 mmol/l;

Arterial hypertension (systolic blood pressure ≥130 mmHg and/or diastolic blood pressure ≥ 85 mmHg) or used drugs for arterial hypertension;

Increased glucose concentration without eating ≥ 5,6 mmol/l or used drugs for the glucose metabolism disorder.

### *6.2.6 Methods of statistical analysis*

The statistical analysis was performed by using „MS Excel“ and „SPSS 17.0“ packages. The data of descriptive statistics was presented in the work: these are arithmetic means of indexes (M), standard deviation (SD), minimal (min) and maximal (max) values of indexes, confidence interval (CI), odds ratio (OR). The statistic relation of the qualitative marks was assessed according to Pearson's ($\chi^2$) criterion. The differences in the parameter criteria between the groups were assessed by using the analytical method ANOVA or according to Student's *t* criterion. The analysis results are to consider statistic-significant in case the value of the chance of an error $p < 0,05$ and very significant in case the value of the chance of an error $p < 0,001$.

## *6.3 Ethical aspects*

The second research was performed after getting the permission from the Lithuanian Bioethics Committee and by following the requirements of the appropriate legal acts. All the participants of that research had been informed about the intended research in writing and signed their agreement to participate in the research.

# 7. RESULTS

## 7.1 Characteristic of the researched

75,1 percent of the participants of the first research were 21–30 years old during the research (mean – 26,9, from 18,6 to 40,5). 64,2 percent women gave the first birth, 35,8 per cent gave repeated birth.

73,3 percent participants of the second research were 40,1–50,0 years old (mean – 47,3, from 39,3 to 62,5). The women gave from 1 to 5 births, 35 women (58,33 percent) gave 2 births. Almost one third of the researched (19 women) had menopause (self- or iatrogenic).

In order to avoid random assessment of our researches, we compared various parameters for the women who came for the repeated research (N=60) and the women of the total primary group and the parameters determined during the first research for the women who did not participate in the second research (tables 3 and 4).

**Table 3**: Comparison of age, body mass, height and BMI of the researched and their neonates' body mass

| Parameters / Groups of women | N | Age, m | Body mass, kg | Height, cm | BMI | Neonate's body mass, g |
|---|---|---|---|---|---|---|
| Researched group | 60 | 26,2 | 62,8 | 164,9 | 23,06 | 3470 |
| Women who were not researched repeatedly | 326 | 25,7 | 63,1 | 164,6 | 23,30 | 3538 |
| Group of first research | 386 | 25,8 | 63,1 | 164,7 | 23,26 | 3537 |
| p * (60/326) | | 0,40 | 0,83 | 0,71 | 0,65 | 0,59 |
| p * (60/386) | | 0,48 | 0,86 | 0,75 | 0,69 | 0,65 |

*) p according to Student's t criterion

**Table 4**: Comparison of the ratio between the women who gave the first and repeated birth

| Parameters / Groups of women | Total | Parity | | | |
|---|---|---|---|---|---|
| | | Giving first birth | | Giving repeated birth | |
| | N | N | Per cent | N | Per cent |
| Researched group | 60 | 37 | 61,7 | 23 | 38,3 |
| Women who were not researched repeatedly | 324 | 206 | 63,6 | 118 | 36,4 |
| Group of first research | 384 | 243 | 63,3 | 141 | 36,7 |
| p * (60/324) | | | | | 0,78 |
| p * (60/384) | | | | | 0,81 |

*) p according to $\chi^2$ criterion

*Note.* In the first research group, the data of 384 women was assessed and in the group of the women who were not researched repeatedly the data of 324 women was researched as the obstetric anamneses of two women were not comprehensive.

The presented data shows the age and anthropometric data of the women of the researched group (N=60) does not differ from analogical data of the women who did not participate in the second research (N=326) or from the total group of the first research (N=386). There was no statistic-significant difference between the proportions of the women giving the first and repeated birth in these groups.

The women of the researched group gave birth to 39 per cent boys and 61 per cent girls, the women who were not repeatedly researched birth to 47,2 per cent boys and 52,8 per cent girls, respectively. The difference between the groups according to $\chi^2$ criterion is statistic-insignificant (p=0,24).

Thus, the analysis of the data of 1986-1987 shows there are no statistic-significant differences between the groups in all the analysed cases. Therefore, it is possible to state the group of women of the second research is representative in respect of the total primary group and the research data and conclusions below can be also applied to the total primary group.

## 7.2 Long-term changes in the women's body

### *7.2.1 Changes in anthropometric parameters of researched women within twenty years*

**Height.** During the first research, the average women's height was 165,0 cm (SD=4,9; min-max 151–176) and 20 years later it was 164,9 cm (SD=4,8; min-max 151–172), p=0,88. When assessing individual height changes, we determined 80 percent women had the same height index during the both researches, the difference in height in 15 percent was only 1 cm and one woman's height (1,66 per cent) decreased by even 8 cm (this woman had rheumatoid arthritis for many years and degenerative changes developed in her joints).

**Body mass.** During the first research, the average women's body mass was 62,7 kg (SD=10,8; min-max 40,0–93,0), and 20 years later it was 74,0 kg (SD=14,3; min-max 42,2–110,3), p<0,001.

We assessed individual changes in the women's body mass (table 5). Among the repeatedly-researched women, there were only five (8,3 per cent) whose body mass decreased a little within 20 years (1,2–4,7 kg). The body mass of 55 other researched (91,7 per cent) increased. The average positive change in the body mass within 20 years kūno was 12,5 kg.

**Table 5**: Women's distribution according to individual changes in the body mass 20 years later

| Changes in the body mass | | N | Percent |
|---|---|---|---|
| Decreased | | 5 | 8,3 |
| Increased (kg) | <5,0 | 10 | 16,7 |
| | 5,1–10,0 | 16 | 26,7 |
| | 10,1–15,0 | 11 | 18,3 |
| | 15,1–20,0 | 7 | 11,7 |
| | 20,1–25,0 | 7 | 11,7 |
| | >25,0 | 4 | 6,7 |
| Total | | 60 | 100,0 |

**BMI.** The average BMI index in the women in early pregnancy was 22,99 (SD=3,65; min-max 17,09–34,58) and twenty years later – 27,17 (SD=4,97; min-max 18,03–37,77), p<0,001. The distribution of the researched women according to the classification intervals of BMI in early pregnancy and 20 later is presented in table 6.

**Table 6**: Women's distribution according to the classification intervals of BMI

| Classification interval of BMI, kg/m² | Research I | | Research II | |
|---|---|---|---|---|
| | N | Percent | N | Percent |
| ≤ 24,99 | 46 | 76,7 | 24 | 40 |
| 25,00–29,99 | 11 | 18,3 | 18 | 30,0 |
| ≥ 30,0 | 3 | 5,0 | 18 | 30,0 |
| Total | 60 | 100,0 | 60 | 100,0 |

**Skin folds.** We analyzed the changes in skin folds in the women within 20 years (table 7). We determined only the chest skin fold thickened statistic-significantly – from 8,5 mm (SD=3,9, min-max 3,0–22,0) to 11,9 mm (SD=4,8, min-max 5,0–42,0) (p<0,001). Abdominal, triceps, femoral and calf skin folds statistic-significantly thinned.

**Table 7**: Thicknesses of skin folds in early pregnancy and 20 years later, mm

| Skin fold, mm | Research I | | Research II | | p |
|---|---|---|---|---|---|
| | M±SD | Min-max | M±SD | Min-max | |
| Chin | 10,3±3,1 | 4,4–18,0 | 9,8±2,8 | 4,6–16,3 | 0,33 |
| Subscapular | 16,2±8,1 | 6,0–39,4 | 17,6±6,9 | 7,1–34,0 | 0,31 |
| Chest | 8,5±3,9 | 3,0–22,0 | 11,9±4,8 | 5,0–42,0 | **<0,001** |
| Abdominal | 27,8±11,6 | 8,2–70,0 | 22,1±8,5 | 7,4–38,4 | **0,003** |
| Triceps | 20,4±8,4 | 9,2–42,0 | 16,0±4,0 | 9,2–28,1 | **<0,001** |
| Biceps | 11,3±6,7 | 3,2–42,0 | 11,0±4,2 | 4,4–24,6 | 0,77 |
| Femoral | 38,4±16,3 | 6,3–80,0 | 23,5±6,1 | 12,3–36,5 | **<0,001** |
| Calf | 20,9±8,9 | 6,0–45,0 | 14,5±4,6 | 7,4–25,0 | **<0,001** |

We assessed the way of changing in the relative part of each skin fold in the total amount of the skin fold indexes within 20 years. The amount of the indexes of all eight skin folds was compared to 100 percent and the relative part of each skin fold was calculated in early pregnancy and 20 years later. We determined the relative part of separate skin folds changed in very different ways (table 8).

**Table 8**: Relative part of the total amount of skin folds

| Skin fold, percent | Research I | | Research II | | p |
|---|---|---|---|---|---|
| | M±SD | Min-max | M±SD | Min-max | |
| Chin | 7,0±1,8 | 4,3–15,1 | 7,8±2,0 | 4,4–14,3 | **0,02** |
| Subscapular | 10,4±2,8 | 5,6–21,4 | 13,7±3,3 | 7,0–23,9 | <**0,001** |
| Chest I | 5,6±1,7 | 2,6–9,6 | 9,3±2,1 | 4,7–13,5 | <**0,001** |
| Abdominal | 18,0±4,1 | 10,0–27,3 | 17,1±4,3 | 8,6–29,5 | 0,24 |
| Triceps | 13,3±2,7 | 8,1–22,6 | 12,8±1,7 | 9,8–16,6 | 0,24 |
| Biceps | 7,1±2,2 | 3,3–15,1 | 8,6±2,0 | 4,7–13,0 | <**0,001** |
| Femoral | 24,8±5,4 | 4,6–36,9 | 19,0±4,2 | 10,1–28,9 | <**0,001** |
| Calf | 13,8±4,3 | 4,5–26,0 | 11,6±2,5 | 5,9–19,9 | <**0,001** |
| Amount of thickness of eight skin folds | 100 | | 100 | | - |

We determined the part of only two skin folds – abdominal and triceps – did not change in the total subcutaneous adipose tissue mass statistic-reliably. The relative part of four skin folds changed statistic-significantly in the total amount of the subcutaneous adipose tissue: chin, subscapular, chest and triceps skin folds. The percentage of the femoral and calf skin folds decreased statistic-significantly.

**Amounts of skin folds and their interrelations.** We assessed the amounts of the skin fold parameters (table 9).

**Table 9**: Amounts of skin folds

| Amount of skin folds, mm | Research I | | Research II | | p |
|---|---|---|---|---|---|
| | M±SD | Min-max | M±SD | Min-max | |
| Eight skin folds | 153,9± 54,3 | 72,8–279,0 | 126,5± 31,8 | 70,6–198,9 | **0,0011** |
| Skin folds of the upper part of body | 66,8± 26,3 | 32,0–139,0 | 66,4± 19,1 | 35,7–117,1 | 0,93 |
| Skin folds of the lower part of body | 87,1± 31,3 | 40,0–154,0 | 60,1± 15,1 | 31,7–89,1 | **<0,001** |
| Torsio skin folds | 62,8± 23,8 | 25,9–141,6 | 61,4± 19,8 | 27,1–102,2 | 0,73 |
| Skin folds of the upper part of torsio | 24,8± 11,5 | 11,0–57,4 | 29,8± 10,7 | 12,1–25,0 | **0,0173** |
| Limb skin folds | 91,0± 34,7 | 43,8–183,0 | 65,1± 15,8 | 37,4–106,9 | **<0,001** |
| Amount of skin folds of the upper limb | 31,7± 14,1 | 14,3–83,0 | 27,0± 9,1 | 14,6–52,7 | **0,011** |
| Amount of skin folds of the lower limb | 60,2± 22,7 | 27,0–116,0 | 38,0± 9,8 | 20,3–59,5 | **<0,001** |

We determined the amount of eight skin folds decreased statistic-reliably within 20 years. It shows the total subcutaneous adipose tissue mass decreased during the researched period.

The amount of skin folds of the upper part of the body and the amount of torsio skin folds did not statistically change within 20 years. However, when assessing analogical indexes of only the upper part of the waist separately, we determined a statistic-significant increase and the amounts of all the other analyzed skin folds decreased statistic-significantly.

The distribution of the subcutaneous adipose tissue in different body parts in the women was assessed according to the relative data of the amounts of skin folds in different body regions. The statistic data analysis shows all the relative anthropometric

indexes chosen for the researched women greatly increased within 20 years (p<0,001) (table 10).

**Table 10**: The amounts of skin folds ratios.

| Relations between the amounts of skin folds | Research I | | Research II | | p |
|---|---|---|---|---|---|
| | M±SD | Min-max | M±SD | Min-max | |
| The amount of skin folds of the upper part of the body and the amount of skin folds of the lower part of the body ratio | 0,79± 0,20 | 0,48–1,49 | 1,12± 0,24 | 0,70–1,87 | **<0,001** |
| The amount of waist skin folds and the amount of limb skin folds ratio | 0,72± 0,22 | 0,40–1,74 | 0,95± 0,27 | 0,49–1,87 | **<0,001** |
| The amount of skin folds of the upper part of the body and the amount of eight skin folds ratio | 0,16± 0,04 | 0,09–0,29 | 0,23± 0,04 | 0,15–0,35 | **<0,001** |

**Passive body mass and its indexes.** We researched the changes in the passive body mass parameters (table 11).

We determined the relative passive body mass in the women decreased statistic-significantly within 20 years. The same passive body mass expressed in the absolute numbers and the Fat mass Ratio did not change statistic-significantly.

**Table 11**: Passive body mass parameters

| Passive body mass indexes | Research I | | Research II | | p |
|---|---|---|---|---|---|
| | M±SD | Min-max | M±SD | Min-max | |
| Passive body mass, per cent | 36,5±3,9 | 25,2–45,1 | 26,8±2,9 | 22,2–33,1 | **<0,001** |
| Passive body mass, kg | 18,6±6,6 | 9,7–40,6 | 20,1±5,6 | 10,2–36,5 | 0,19 |
| Fat mass Ratio, kg/m² | 6,8±2,4 | 4,1–15,1 | 7,2±2,2 | 4,3–12,3 | 0,34 |

**Body circumferences.** During the first research, the determined mean of the chest circumference was 87,9 cm (SD=6,1, min-max 74–102), twenty years later it was 102,5 cm (SD=12,2, min-max 79,0–128,0), p<0,001.

During the first research, the determined mean of the abdominal circumference was 83,7 cm (SD=8,5 cm; min-max 67–105,0), twenty years later it was 88,1 cm (SD=13,4 cm; min-max 63,0–115,0), p=0,04.

### *7.2.2 Changes in metabolism of researched women within twenty years*

#### *7.2.2.1 Changes in lipid metabolism parameters*

We assessed the changes in the lipid metabolism (table 12).

**Table 12**: Lipid metabolism parameters

| Lipid metabolism parameters | Research I | | Research II | | p |
|---|---|---|---|---|---|
| | M±SD | Min-max | M±SD | Min-max | |
| Ch, mmol/l | 5,07±1,01 | 3,49–8,00 | 5,61±0,95 | 3,24–7,68 | **<0,001** |
| HDL cholesterol, mmol/l | 1,78±0,67 | 0,65–4,26 | 1,71±0,48 | 0,89–4,50 | 0,66 |
| LDL cholesterol, mmol/l | 2,43±0,97 | 0,19–4,44 | 3,52±0,88 | 1,80–5,27 | **<0,001** |
| Tg, mmol/l | 1,81±0,77 | 0,51–4,62 | 1,09±0,41 | 0,33–2,17 | **<0,001** |
| VLDL cholesterol, mmol/l | 0,89±0,43 | 0,11–2,12 | 0,51±0,24 | 0,09 –1,02 | **<0,001** |
| non-HDL cholesterol, mmol/l | 3,28±1,08 | 0,69– 5,53 | 3,86±1,00 | 1,49–5,88 | **0,003** |
| LDL/HDL | 1,67±1,20 | 0,04– 5,23 | 2,21±0,76 | 0,91–3,84 | **0,006** |
| Ch/HDL | 3,22±1,33 | 1,16–7,17 | 3,49±0,88 | 1,47–5,45 | 0,21 |
| Tg/HDL | 1,09±0,50 | 0,28–2,36 | 0,70±0,34 | 0,21–1,63 | **<0,001** |
| AC | 2,20±1,33 | 0,16–6,17 | 2,49±0,88 | 0,47–4,45 | 0,18 |
| AIP | -0,01±0,20 | -0,55–0,37 | -0,20±0,21 | -0,68–0,21 | **<0,001** |

The total Ch concentration not only increased statistic-significantly in the researched women within 20 years, but also exceeded the physiologic norm limits, i.e., it reached atherogenic values. This increase in the total Ch concentration occurred due to a growth in LDL cholesterol – the changes in its concentration are analogical and the mean

20 later exceeds the physiological norm limits. The means of the total Ch and LDL cholesterol concentrations even exceed more liberal recommended limits [170].

We did not find any statistic-significant changes in HDL cholesterol concentration within 20 years. Tg concentration decreased statistic-reliably within 20 years.

Among the researched derived lipid metabolism indexes, two of them – Ch/HDL cholesterol and AC – did not change statistic-significantly. The other derived indexes changed statistic-reliably: the VLDL cholesterol concentration decreased, non-HDL cholesterol concentration increased, LDL /HDL ratio increased, Tg/HDL ratio decreased and AIP increased.

#### *7.2.2.2 Changes in glucose metabolism within twenty years*

We assessed the changes in the glucose concentration within 20 years (table 13).

**Table 13**: Glucose concentration, mmol/l

| | Glucose | |
|---|---|---|
| | Research I | Research II |
| M±SD | 3,67±0,69 | 5,26±0,72 |
| Min-max | 2,50–5,50 | 1,93–6,64 |
| p | | **<0,001** |

The glucose concentration increased statistic-significantly within 20 years. In early pregnancy, even the maximal concentrations did not exceed the physiological norm limits. 20 years later, the mean of the glucose concentration approached to the values of the diagnostic criterion of MS and the maximal values exceeded the physiological norm limits.

During the second research, we assessed the researched women's resistance to insulin by calculating HOMA-IR index. We found the mean of HOMA-IR index in the researched women was 1,82 (SD=1,44, min-max 0,39–7,04). These values of HOMA-IR index coincide with the norm limits, but in 17 women (28,33 per cent) HOMA-IR index exceeds the value of 2,1, in 12 women of them (20 percent) this index exceeds the value of 2,7 and in 5 women (8,33 percent) – the value of 4,64. Thus, it is possible to state increased resistance to insulin is even characteristic to one fifth of the researched women.

### *7.2.2.3 Relation between changes in anthropometric and metabolic parameters in women and tendency to have metabolic syndrome*

We assessed the influence by a significantly increased body mass on the carbohydrate metabolism. We compared HOMA-IR index in the women whose classification interval of BMI had not changed and those whose classification interval of BMI had changed from the norm to obesity (table 14). In the women whose body mass had increased from the norm to obesity within 20 years, increased resistance to insulin was found. Their HOMA-IR mean is not only statistic-significantly higher than in those women whose classification interval of BMI had not changed within 20 years, but it largely exceeds the physiological norm limits.

**Table 14**: HOMA-IR index

| | HOMA-IR | |
|---|---|---|
| | I * | II** |
| N | 28 | 7 |
| M±SD | 1,34±1,03 | 3,19±1,73 |
| Min-max | 0,44–4,64 | 1,04–5,67 |
| p | | **0,03** |

*) I – group of women whose BMI stayed in the same classification interval within 20 years;

**) II – group of women whose body mass increased from the norm to obesity within 20 years.

We assessed the relation between the change in the classification interval of BMI and frequency of MS. By applying $\chi^2$ analysis, we determined the women whose classification interval of BMI had increased within 20 years, had a statistic-significant higher possibility to have MS (p=0,0001) compared with those who stayed in the same classification interval of BMI.

## 7.3 Peculiarities of anthropometric and metabolic changes in healthy and metabolic syndrome women during pregnancy and within twenty years

We assessed the frequency of MS in the group of the researched women. It was determined 22 women (36,7 percent) had MS.

### *7.3.1 Peculiarities of anthropometric changes in healthy and metabolic syndrome women during pregnancy and within twenty years*

We assessed the **height** of the researched women in early pregnancy and 20 years later. There are no statistic-significant height differences between MS (+) and MS (-) (table 15).

**Table 15**: Height of healthy and MS women

| Height, cm | In early pregnancy | | 20 years later | |
|---|---|---|---|---|
| | MS (+) | MS (-) | MS (+) | MS (-) |
| M±SD | 165,2±4,5 | 164,9±5,2 | 165,5±4,5 | 164,6±5,0 |
| Min-max | 154,0–172,0 | 151,0–176,0 | 154,0–172,0 | 154,0–170,0 |
| p | 0,81 | | 0,48 | |

We assessed the **women's body mass and BMI** in MS (+) and MS (-) (table 16).

**Table 16**: Body mass and BMI in healthy and MS (+) women

| | | In early pregnancy | | In late pregnancy | | 20 years later | |
|---|---|---|---|---|---|---|---|
| | | MS (+) | MS (-) | MS (+) | MS (-) | MS (+) | MS (-) |
| Body mass, kg | M±SD | 69,2±10,7 | 59,0±9,0 | 82,8±9,2 | 72,6±7,4 | 86,4±9,6 | 66,8±11,5 |
| | Min-max | 56,0–93,0 | 40,0–80,2 | 70,8–105,0 | 50,8–85,3 | 70,8–110,3 | 42,2–94,9 |
| | p | **<0,001** | | **<0,001** | | **<0,001** | |
| BMI, kg/m² | M±SD | 25,3±3,7 | 21,6±2,9 | 30,0±3,1 | 26,4±2,0 | 31,6±3,4 | 24,6±3,8 |
| | Min-max | 19,38–34,58 | 17,09–32,13 | 25,71–39,04 | 21,70–29,82 | 25,50–37,38 | 18,03–37,77 |
| | p | **<0,001** | | **<0,001** | | **<0,001** | |

The body mass of MS (+) women was statistic-significantly higher than of MS (-) already in early pregnancy. A statistic-significant difference in the body mass between the groups also remains in late pregnancy and 20 years later.

We found analogical statistic-significant differences in BMI between the groups. In early pregnancy the mean of BMI in MS (-) women is 21,6 and coincides with the classification interval of BMI of the physiological norm and in MS (+) women the mean of BMI coincides with the classification interval of overweight BMI already in early pregnancy – 25,3. In late pregnancy the mean of BMI in MS (+) women was 30,0 and coincided with the criteria of obesity recommended for the determination of obesity

during pregnancy [95, 96]. In the healthy women, even the maximal values of BMI did not reach analogical values in late pregnancy.

Thus, MS (+) women's body mass and appropriate BMI was higher already 20 years ago – in early and in late pregnancy – compared with MS (-) women.

20 years later the difference between the means of BMI in the groups was statistic-significant. The minimal values of BMI in MS (+) women exceeded the limits of the classification interval of BMI of the physiological norm – the mean is 31,6; the mean of BMI parameters in healthy women coincides with the values of the classification interval of BMI of the physiological norm – 24,6.

We assessed the **chest and abdominal circumferences** in the researched women (table 17).

**Table 17**: Chest and abdominal circumferences in healthy and MS (+) women

| Circumferences, cm | | In early pregnancy | | In late pregnancy | | 20 years later | |
|---|---|---|---|---|---|---|---|
| | | MS (+) | MS (-) | MS (+) | MS (-) | MS (+) | MS (-) |
| Chest | M± SD | 91,0± 5,0 | 85,7± 5,9 | 95,8± 3,4 | 90,5± 5,0 | 113,7± 7,8 | 96,0± 9,3 |
| | Min-max | 83,0–102,0 | 74,0–102,0 | 92,0–104,0 | 78,0–103,0 | 100,0–128,0 | 79,0–120,0 |
| | p | | **<0,001** | | **<0,001** | | **<0,001** |
| Abdominal | M± SD | 88,6± 7,1 | 80,7± 8,0 | 107,1± 5,1 | 99,3± 6,3 | 101,4± 8,0 | 80,4± 9,3 |
| | Min–max | 77,0–99,0 | 67,0–105,0 | 101,0–117,0 | 85,0–116,5 | 86,0–115,0 | 63,0–104,0 |
| | p | | **<0,001** | | **<0,001** | | **<0,001** |

The both body circumferences in MS (+) women were statistic-significantly higher than analogical parameters in the healthy women during each research period.

We assessed the **changes in the chest and abdominal circumferences** from early pregnancy to the end of the research 20 years later. The chest circumference changed statistic-significantly from early pregnancy within 20 years in the both groups – MS (+) and MS (-) (in the both cases $p<0,001$). The changes in the abdominal circumference were different in the healthy and MS (+) women. The abdominal

circumference in the healthy women did not change statistic-significantly (p=0,88); the abdominal circumference largely increased in MS (+) women (p <0,001).

**Skin folds.** We analyzed the differences in skin folds between MS (+) and MS (-) women during each research period (table 18).

**Table 18**: Skin folds in healthy and MS (+) women, mm

| Skin folds | | In early pregnancy | | In late pregnancy | | 20 years later | |
|---|---|---|---|---|---|---|---|
| | | MS (+) | MS (-) | MS (+) | MS (-) | MS (+) | MS (-) |
| Chin | M±SD | 11,7±3,3 | 9,5±2,7 | 11,4±2,7 | 9,1±2,3 | 11,4±2,3 | 8,8±2,7 |
| | Min-max | 7,3– 18,0 | 4,4–16,0 | 8,0–18,0 | 5,0–15,2 | 8,0–16,3 | 4,6–15,1 |
| | p | **0,01** | | **0,005** | | **<0,001** | |
| Subscapular | M±SD | 21,4±9,1 | 13,2±5,7 | 24,9±9,1 | 15,9±7,0 | 23,8±5,0 | 14,0±5,0 |
| | Min-max | 9,1–39,4 | 6,0–30,3 | 12,1–46,3 | 7,4–38,3 | 16,0–34,0 | 7,1–25,0 |
| | p | **0,001** | | **0,001** | | **<0,001** | |
| Chest I | M±SD | 10,6±3,8 | 7,3±3,5 | 15,1±5,8 | 9,3±4,2 | 15,3±5,1 | 10,0±3,3 |
| | Min-max | 4,4–18,0 | 3,0–22,0 | 8,3–33,0 | 4,0–27,0 | 6,4–24,2 | 5,0–18,1 |
| | p | **0,002** | | **<0,001** | | **<0,001** | |
| Abdominal | M±SD | 34,1±11,2 | 24,2±10,4 | 31,3±12,5 | 19,3±7,4 | 28,9±6,3 | 18,1±7,1 |
| | Min-max | 19,0–70,0 | 8,2–45,0 | 14,2–65,0 | 10,2–46,1 | 15,4–38,4 | 7,4–33,4 |
| | p | **0,002** | | **0,001** | | **<0,001** | |
| Triceps | M±SD | 24,2±8,8 | 18,3±7,5 | 26,6±9,2 | 16,6±7,1 | 18,7±4,2 | 14,4±2,9 |
| | Min-max | 11,2–42,0 | 9,2–40,1 | 16,0–45,3 | 7,2–45,3 | 12,0–28,1 | 9,2–22,0 |
| | p | **0,01** | | **<0,001** | | **<0,001** | |
| Biceps | M±SD | 14,1±8,3 | 9,7±5,0 | 15,1±8,8 | 8,5±4,4 | 13,7±4,8 | 9,3±2,7 |
| | Min-max | 4,2– 42,0 | 3,2–26,0 | 5,0–37,1 | 3,4–26,0 | 6,4–24,6 | 4,4–15,0 |
| | p | **0,03** | | **0,007** | | **<0,001** | |
| Femoral | M±SD | 45,2±19,2 | 34,4±13,2 | 61,8±16,2 | 40,7±18,3 | 24,7±6,3 | 22,9±6,0 |
| | Min-max | 6,3–80,0 | 15,1–70,0 | 32,0–85,0 | 19,2–90,0 | 12,3–35,0 | 13,0–36,5 |
| | p | **0,03** | | **<0,001** | | 0,27 | |
| Calf | M±SD | 21,9±8,6 | 20,3±9,2 | 23,0±8,2 | 19,7±8,2 | 16,6±5,4 | 13,3±3,6 |
| | Min-max | 6,0–37,0 | 7,2–45,0 | 10,1–44,4 | 7,2–40,0 | 7,4–25,0 | 8,0–24,3 |
| | p | 0,49 | | 0,16 | | **0,02** | |

Almost all skin folds in MS (+) women are bigger already in early pregnancy compared with analogical indexes in MS (-) women (p=0,03–0,001). We did not only find a statistic-reliable difference when measuring the calf skin fold (p=0,49), but the tendency of differences between the groups is similar.

We also found analogical statistic-significant differences between appropriate skin folds in late pregnancy. Almost all skin folds in MS (+) women are bigger in late pregnancy compared with analogical indexes in the healthy ones.

20 years later a statistic-significant difference in the femoral skin folds between the groups decreased and a significant difference in the calf skin fold appeared. The relation between other skin folds remained the same – skin folds in MS (+) women are significantly bigger than appropriate parameters in MS (-) women.

We determined the changes in skin folds were not proportional:

- The chin and abdominal skin folds decrease from their primary value until the end of pregnancy and 20 years later we find these parameters are even more decreased;
- The subscapular and chest skin fold increase until the end of pregnancy and 20 years later the values are lower than in late pregnancy, but bigger than in early pregnancy;
- The femoral skin fold increases from the primary values until the end of pregnancy and significantly decreases 20 years later.

These changes are noticed in MS (+) and MS (-) women.

Another kind of tendency is characteristic to the other folds – triceps, biceps and calf ones. These skin folds tend to decrease until the end of pregnancy in healthy women and increase in MS (+) women. Thus, these changes show the decentralization of the fatty tissue in MS (+) women during pregnancy.

We assessed the **relative expression of each skin fold** from early pregnancy. In case the thickness of each skin fold measured in early pregnancy is compared to 100 percent, the relative expression of each skin fold is different in late pregnancy and 20 years later (table 19).

On the contrary to the case of thicknesses of absolute skin folds, when assessing the percent expression of the fold in late pregnancy, we only found a statistic-reliable difference of the triceps fold (p=0,01). The relative expression of the triceps skin fold increases in MS (+) women in late pregnancy (its value exceeds 100 percent) and the same skin fold decreases in healthy women (its value is less than 100 percent). Thus, the tendency of the changes in the relative expression of the triceps skin fold in MS (+)

women during pregnancy reflects the general tendency of decentralization of the subcutaneous adipose tissue.

**Table 19**: Relative indexes of skin folds in healthy and MS (+) women

| Skin folds, percent | | In late pregnancy | | 20 years later | |
|---|---|---|---|---|---|
| | | MS (+) | MS (-) | MS (+) | MS (-) |
| Chin | M±SD | 98,6±21,5 | 97,7±16,1 | 105,1±32,8 | 96,8±28,1 |
| | Min-max | 58,1–138,2 | 50,0–140,0 | 50,0–149,4 | 31,9–160,0 |
| | p | 0,87 | | 0,33 | |
| Subscapular | M±SD | 124,0±35,0 | 122,0±20,6 | 126,2±43,6 | 112,4±33,8 |
| | Min-max | 84,0–220,5 | 85,3–185,4 | 52,8–224,2 | 57,1–191,2 |
| | p | 0,83 | | 0,21 | |
| Chest | M±SD | 157,7±86,4 | 133,5±42,4 | 156,1±59,7 | 157,1±77,0 |
| | Min-max | 66,7–471,4 | 66,7–267,7 | 63,6–295,5 | 50,0–451,6 |
| | p | 0,27 | | 0,96 | |
| Abdominal | M±SD | 98,5±41,9 | 84,3±23,2 | 90,4±27,5 | 85,0±45,9 |
| | Min-max | 36,3–224,1 | 42,4–158,5 | 44,0–153,6 | 30,3–285,4 |
| | p | 0,19 | | 0,57 | |
| Triceps | M±SD | 114,0±27,0 | 93,9±24,0 | 85,3±31,2 | 90,1±31,9 |
| | Min-max | 70,3–177,5 | 46,7–153,3 | 33,3–169,6 | 37,7–164,0 |
| | p | **0,01** | | 0,58 | |
| Biceps | M±SD | 111,5±41,6 | 94,4±29,9 | 118,4±60,8 | 112,0±43,4 |
| | Min-max | 50,0–193,8 | 45,0–170,0 | 33,0–267,6 | 38,8–206,8 |
| | p | 0,13 | | 0,67 | |
| Femoral | M±SD | 134,8±54,6 | 122,2±50,9 | 59,6±31,7 | 73,1±26,2 |
| | Min-max | 53,3–285,0 | 65,2–364,2 | 29,2–162,7 | 33,3–145,7 |
| | p | 0,41 | | 0,1 | |
| Calf | M±SD | 107,2±30,9 | 102,4±31,6 | 90,1±55,4 | 74,0±28,6 |
| | Min-max | 54,2–168,3 | 48,4–225,0 | 31,6–283,3 | 28,9–181,9 |
| | p | 0,6 | | 0,22 | |

By applying $\chi^2$ analysis, we determined a risk of developing MS within 20 years from the beginning of the research was almost 5 times higher for the women whose triceps skin fold increased during pregnancy (OR=4,73, CI=1,4–15,8, p=0,0092) compared with the women whose triceps skin fold decreased during pregnancy.

**Amounts of skin fold parameters and their ratios.** In order to determine the peculiarities of topographic changes in the subcutaneous adipose tissue in MS (+) and MS (-) women, we assessed the amounts of the skin fold parameters and the amounts of the skin folds ratios, changes in these derived parameters until the end of pregnancy and 20 years later (table 20).

**Table 20**: Amounts of skin folds in healthy and MS (+) women

| Amounts of skin folds, mm | | In early pregnancy | | In late pregnancy | | 20 years later | |
|---|---|---|---|---|---|---|---|
| | | MS (+) | MS (-) | MS (+) | MS (-) | MS (+) | MS (-) |
| Eight skin folds | M± SD | 183,3± 52,4 | 136,9± 48,4 | 209,2± 54,1 | 139,1± 49,6 | 153,2± 23,8 | 110,2± 24,2 |
| | Min-max | 90,0–279,0 | 72,8–275,8 | 138,7–329,0 | 74,4–324,6 | 121,5–198,9 | 70,6–155,5 |
| | p | | **0,002** | | **<0,001** | | **<0,001** |
| Skin folds of the upper part of body | M± SD | 82,0±27,1 | 58,0± 21,6 | 93,1± 30,7 | 59,4± 22,1 | 82,9± 16,0 | 56,3± 12,7 |
| | Min-max | 38,7–139,0 | 32,0–130,5 | 50,4–159,8 | 31,9–151,5 | 58,4–117,1 | 35,7–82,8 |
| | p | | **0,001** | | **<0,001** | | **<0,001** |
| Skin folds of the lower part of body | M± SD | 101,3± 30,0 | 78,9± 29,4 | 116,1± 28,3 | 79,7± 30,5 | 70,2± 12,3 | 54,3± 13,5 |
| | Min-max | 51,3–154,0 | 40,0–145,3 | 70,4–169,2 | 42,5–173,1 | 42,3–89,1 | 31,7–78,5 |
| | p | | **0,007** | | **<0,001** | | **<0,001** |
| Torsio skin folds | M± SD | 77,8± 23,9 | 54,2± 19,3 | 82,6± 26,6 | 53,6± 17,7 | 79,5± 13,5 | 51,0± 14,8 |
| | Min-max | 44,3–141,6 | 25,9–109,4 | 45,4–158,4 | 30,0–126,3 | 54,8–102,2 | 27,1–82,8 |
| | p | | **<0,001** | | **<0,001** | | **<0,001** |
| Limb skin folds | M± SD | 105,5± 36,8 | 82,7± 30,9 | 126,6± 36,3 | 85,5± 34,0 | 73,7± 16,7 | 59,8± 12,9 |
| | Min-max | 45,7–183,0 | 43,8–166,4 | 79,4–211,8 | 41,8–198,3 | 42,3–106,9 | 37,4–93,0 |
| | p | | **0,02** | | **<0,001** | | **0,002** |

We determined statistic-significant differences in the amounts of skin folds between the groups already in early pregnancy. The amount of all eight skin folds and the amounts of skin folds of separate body regions in early pregnancy are higher in MS

(+) women. The differences between the groups are only bigger in late pregnancy as well as 20 years later, p values in the case of all total indexes <0,001.

We assessed the distribution of the subcutaneous fatty tissue in the organism according to the **relative data of the amounts of skin folds of separate body regions** (table 21).

**Table 21**: Ratios between the amounts of skin folds in healthy and MS (+) women

| Ratios between amounts of skin folds | | In early pregnancy | | In late pregnancy | | 20 years later | |
|---|---|---|---|---|---|---|---|
| | | MS (+) | MS (-) | MS (+) | MS (-) | MS (+) | MS (-) |
| U/L* | M±SD | 0,83± 0,23 | 0,76± 0,18 | 0,81± 0,23 | 0,78± 0,19 | 1,21± 0,27 | 1,07± 0,20 |
| | Min-max | 0,49– 1,49 | 0,48– 1,27 | 0,46– 1,36 | 0,44– 1,22 | 0,80– 1,87 | 0,70– 1,70 |
| | p | | 0,22 | | 0,55 | | **0,04** |
| T/Limb** | M±SD | 0,79± 0,28 | 0,67± 0,16 | 0,68± 0,21 | 0,66± 0,16 | 1,13± 0,31 | 0,85± 0,18 |
| | Min-max | 0,40– 1,74 | 0,46– 1,04 | 0,44– 1,09 | 0,41– 1,15 | 0,69– 1,87 | 0,49– 1,25 |
| | p | | 0,09 | | 0,77 | | **<0,001** |
| T/8*** | M±SD | 0,45± 0,06 | 0,43± 0,06 | 0,49± 0,06 | 0,50± 0,06 | 0,54± 0,05 | 0,51± 0,04 |
| | Min-max. | 0,33– 0,60 | 0,32– 0,56 | 0,37– 0,63 | 0,38– 0,60 | 0,44– 0,65 | 0,41– 0,63 |
| | p | | 0,22 | | 0,71 | | **0,04** |

*) U/L – ratio between the amount of skin folds of the upper part of the body and the amount of skin folds of the lower part of the body;

**) T/Limb – ratio between the amount of the waist skin folds land the amount of limb skin folds;

***) T/8 – ratio between the amount of skin folds of the upper part of the waist and the amount of eight skin folds.

We determined all the relative anthropometric parameters chosen for the researched women in early pregnancy and in late pregnancy did not change statistic-significantly. 20 years later statistic-significant differences can be seen in the proportions of distribution of the subcutaneous adipose tissue between MS (+) and MS (-) women. The most obvious differences (p<0,001) were found when assessing the ratios between

the waist and limb skin folds. Thus, the subcutaneous adipose tissue in MS (+) women is clearly centralized compared with the topography of the adipose tissue in MS (-) women.

We assessed the changes in the **passive body mass** parameters in MS (+) and MS (-) women during pregnancy and 20 years later (table 22). We determined MS (+) women had accumulated more passive body mass already from early pregnancy. They can be characterized by a statistic-significant (p<0,001) bigger amount of the passive body mass and its ratio with height. Analogical differences are also found in late pregnancy and 20 years later.

**Table 22**: Passive body mass parameters in healthy and MS (+) women

| Passive body mass parameters | | In early pregnancy | | In late pregnancy | | 20 years later | |
|---|---|---|---|---|---|---|---|
| | | MS (+) | MS (-) | MS (+) | MS (-) | MS (+) | MS (-) |
| Passive body mass, percent | M±SD | 32,0± 5,4 | 27,1± 4,3 | 35,5± 5,3 | 28,4± 5,1 | 29,3± 2,0 | 25,2± 2,2 |
| | Min-max | 22,8–43,7 | 22,2–40,2 | 28,4–46,8 | 22,2–46,8 | 26,7–33,1 | 22,2–30,0 |
| | p | | **<0,001** | | **<0,001** | | **<0,001** |
| Passive body mass, kg | M±SD | 22,6± 7,1 | 16,3± 5,1 | 30,2± 6,9 | 21,1± 6,0 | 25,4± 3,7 | 16,8± 3,9 |
| | Min-max | 14,1–40,6 | 9,7–32,2 | 21,1–46,5 | 13,4–42,6 | 19,8–36,5 | 10,2–25,5 |
| | p | | **<0,001** | | **<0,001** | | **<0,001** |
| Fat mass Ratio, kg/m² | M±SD | 8,27± 2,57 | 5,96± 1,82 | 10,97± 2,49 | 7,70± 2,23 | 9,27± 1,26 | 6,17± 1,26 |
| | Min-max | 4,90–15,09 | 4,13–12,90 | 7,31–17,30 | 5,62–17,07 | 7,20–12,34 | 4,35–8,94 |
| | p | | **<0,001** | | **<0,001** | | **<0,001** |

We calculated the **ratio between an augment in the absolute passive body mass during pregnancy and the neonate's birth mass**. We found a statistic-significant difference (p=0,02) in this derived index between MS (+) and MS (-) women. MS (-) women put on weight by averagely 1,29 kg of the passive body mass for each kilo of their foetus (SD=0,68, min-max 0,51–3,04). MS (+) women weighted almost twice more of the passive body mass for each kilo of the foetus during pregnancy; the average ratio between an augment in the passive body mass and the neonate's birth mass was 2,5 kg

(SD=1,82, min-max 1,25–8,51) among these women. By applying $\chi^2$ analysis, we determined a risk of developing MS until the end of the research was more than 20 times higher for the women who had put on weight more than 1,29 of the passive body mass for each kilo of the foetus (i.e., more than the average of this index in healthy women) during pregnancy compared with those who had put on less weight: OR=22,0, CI=2,6–187,0, p<0,001.

### *7.3.2 Peculiarities of metabolic changes in healthy and metabolic syndrome women during pregnancy and within twenty years*

#### *7.3.2.1 Peculiarities of lipid changes in healthy and metabolic syndrome women during pregnancy and within twenty years*

We determined in early pregnancy and in late pregnancy there was no statistic-significant change between the lipid concentration in MS (+) and MS (-) women (table 23). We noticed the total Ch and Tg concentrations did not reliably differ in MS (+) women compared with analogical indexes in MS (-) women, but they exceeded the physiological norm limits; these indexes stayed in the physiological norm limits in MS (-) women.

When assessing the data received at the end of the research, we found a statistic-significant change (p<0,001) in Tg concentration of the researched women – Tg concentration was higher in MS (+) women compared with an analogical index in the healthy women. Even the maximal values of Tg concentrations in the healthy women coincided with the physiological norm limits.

**Table 23**: The lipid concentration in healthy and MS (+) women

| | | In early pregnancy | | In late pregnancy | | 20 years later | |
|---|---|---|---|---|---|---|---|
| | | MS (+) | MS (-) | MS (+) | MS (-) | MS (+) | MS (-) |
| Ch, mmol/l | M± SD | 5,24± 1,05 | 4,97± 0,99 | 6,90± 1,26 | 6,37± 1,00 | 5,83± 0,81 | 5,36± 1,13 |
| | Min-max | 3,49–7,38 | 3,49–8,00 | 5,24–9,03 | 4,36–9,03 | 3,88–7,68 | 1,91–7,25 |
| | p | 0,32 | | 0,15 | | 0,07 | |
| HDL cholesterol, mmol/l | M± SD | 1,81± 0,65 | 1,76± 0,69 | 2,46± 0,86 | 2,13± 0,71 | 1,53± 0,34 | 1,67± 0,36 |
| | Min-max | 0,65–3,11 | 0,81–4,26 | 1,50–3,93 | 0,98–3,93 | 0,89–2,09 | 0,42–2,24 |
| | p | 0,79 | | 0,2 | | 0,15 | |
| LDL cholesterol, mmol/l | M± SD | 2,50± 0,84 | 2,39± 1,05 | 2,98± 0,84 | 2,85± 0,68 | 3,65± 0,77 | 3,33± 0,97 |
| | Min-max | 0,92–4,00 | 0,19–4,44 | 1,18–4,36 | 1,62–4,51 | 2,30–5,04 | 1,29–4,73 |
| | p | 0,68 | | 0,6 | | 0,17 | |
| Tg, mmol/l | M± SD | 1,97± 0,71 | 1,70± 0,80 | 3,39± 0,79 | 3,13± 0,99 | 1,39± 0,38 | 0,91± 0,32 |
| | Min-max | 0,84–4,43 | 0,51–4,62 | 2,26–4,89 | 1,02–5,84 | 0,86–2,17 | 0,33–1,69 |
| | p | 0,2 | | 0,34 | | **<0,001** | |

During pregnancy, all women's lipid metabolism parameters (total Ch, HDL, LDL and Tg concentrations) increase, but it is a general feature and there are no statistic-significant differences in the data between the groups.

We determined statistic-significant lipid metabolism changes in MS (+) women within a 20-year period: the total Ch concentration increased, p=0,047; LDL cholesterol concentration increased, p<0,001; Tg concentration decreased, p=0,02. In MS (+) women, HDL cholesterol concentration did not change significantly. Tg concentration statistic-reliably decreased in healthy women (p<0,001), the changes in other lipids profile parameters are statistic-unreliable.

Thus, we determined the changes in the lipid metabolism in MS (+) women within two decades had a more expressed tendency which was not favourable in the atherogenic aspect.

We calculated **derived lipid profile parameters** (table 24). In early pregnancy and in late pregnancy, the derived lipid metabolism parameters which were researched in MS (+) and MS (-) women did not change statistic-significantly. 20 years later all the researched parameters are statistic-significantly higher in MS (+) women compared with analogical indexes in the healthy women.

**Table** 24: Derived lipid metabolism parameters in healthy and MS (+) women

| | | In early pregnancy | | In late pregnancy | | 20 years later | |
|---|---|---|---|---|---|---|---|
| | | MS (+) | MS (-) | MS (+) | MS (-) | MS (+) | MS (-) |
| VLDL cholesterol, mmol/l | M±SD | 0,96±0,32 | 0,84±0,48 | 1,55±0,36 | 1,39±0,44 | 0,67±0,22 | 0,41±0,20 |
| | Min-max | 0,61–2,03 | 0,11–2,12 | 1,04–2,23 | 0,47–2,67 | 0,32–1,02 | 0,09–0,99 |
| | p | 0,27 | | 0,19 | | **<0,001** | |
| non-HDL cholesterol, mmol/l | M±SD | 3,46±0,97 | 3,18±1,14 | 4,53±1,11 | 4,24±0,84 | 4,37±0,90 | 3,78±1,02 |
| | Min-max | 1,84–5,46 | 0,69–5,53 | 2,22–6,23 | 2,58–6,06 | 2,99–6,60 | 1,49–5,54 |
| | p | 0,33 | | 0,37 | | **0,02** | |
| LDL /HDL | M±SD | 1,70±1,20 | 1,66±1,22 | 1,37±0,62 | 1,52±0,74 | 2,51±0,81 | 2,08±0,70 |
| | Min-max | 0,30–5,23 | 0,04–4,83 | 0,33–2,67 | 0,45–4,34 | 1,48–3,84 | 0,91–3,77 |
| | p | 0,91 | | 0,48 | | **0,05** | |
| Ch/HDL | M±SD | 3,30±1,42 | 3,16±1,30 | 3,07±0,87 | 3,25±1,02 | 3,93±0,85 | 3,34±0,77 |
| | Min-max | 1,59–7,17 | 1,16–6,33 | 1,62–4,82 | 1,78–7,13 | 2,69–5,45 | 2,02–4,97 |
| | p | 0,72 | | 0,55 | | **0,01** | |
| Tg/ HDL | M±SD | 1,19±0,50 | 1,02±0,49 | 1,53±0,61 | 1,63±0,79 | 0,97±0,36 | 0,57±0,23 |
| | Min-max | 0,64–2,31 | 0,28–2,36 | 0,63–2,52 | 0,35–4,46 | 0,45–1,63 | 0,21–1,05 |
| | p | 0,21 | | 0,63 | | **<0,001** | |
| AC | M±SD | 2,30±1,42 | 2,15±1,29 | 2,07±0,87 | 2,25±1,02 | 2,93±0,85 | 2,35±0,80 |
| | Min-max | 0,59–6,17 | 0,16–5,33 | 0,62–3,82 | 0,78–6,13 | 1,69–4,45 | 1,02–3,97 |
| | p | 0,68 | | 0,55 | | **0,02** | |
| AIP | M±SD | 0,04±0,17 | -0,04±0,22 | 0,15±0,18 | 0,17±0,20 | -0,04±0,17 | -0,28±0,19 |
| | Min-max | -0,19–0,36 | -0,55–0,37 | -0,20–0,40 | -0,46–0,65 | -0,35–0,21 | -0,68–0,02 |
| | p | 0,12 | | 0,77 | | **<0,001** | |

### *7.3.2.2 Peculiarities of glucose changes in healthy and metabolic syndrome women during pregnancy and within twenty years*

We assessed the **glucose concentration** in MS (+) and MS (-) women in early pregnancy, in late pregnancy and 20 years later (table 25).

**Table 25:** Glucose concentration in healthy and MS (+) women

| Glucose, mmol/l | In early pregnancy | | In late pregnancy | | 20 years later | |
|---|---|---|---|---|---|---|
| | MS (+) | MS (-) | MS (+) | MS (-) | MS (+) | MS (-) |
| M±SD | 3,89±0,87 | 3,53±0,53 | 3,60±0,77 | 3,39±0,71 | 5,75±0,50 | 4,98±0,69 |
| Min-max | 2,50–5,50 | 2,60–4,80 | 2,70–5,20 | 1,80–4,85 | 4,75–6,64 | 1,93–5,99 |
| p | 0,13 | | 0,39 | | **<0,001** | |

We determined there is no statistic-significant difference in the glucose concentration between the groups in early pregnancy and in late pregnancy. 20 years later, the glucose concentration in MS (+) women is statistic-significantly higher compared with the healthy women ($p<0,001$).

## 7.4 Peculiarities of leptin and adiponectin metabolism in women under physiological and pathological conditions

We assessed the leptin and adiponectin concentrations in serum for the women. We also calculated two derived indexes: the ratio between the leptin concentration and adiponectin concentration and the ratio between the adiponectin concentration and BMI.

The data of the adipokines metabolism parameters is presented in table 26.

**Table 26**: Leptin and adiponectin concentrations, leptin/adiponectin ratio and adiponectin/BMI ratio

| | Leptin, ng/ml | Adiponectin, μg/ml | Leptin/ adiponectin | Adiponectin/ BMI |
|---|---|---|---|---|
| M± SD | 14,3±7,5 | 23,9±14,31 | 0,85±0,68 | 0,93±0,67 |
| Min-max | 2,4–32,1 | 8,53–85,08 | 0,06–2,85 | 0,27–4,29 |

The mean of the leptin concentration in the women is 14,3 ng/ml, it coincides with the physiological norm limits. The leptin concentration in one woman (1,7 percent) is less than the lower limit of the norm, in 15 women (25 percent) this parameters is

higher than the upper limit of the norm. The average parameters of the adiponectin concentration is 23,9 μg/ml and the minimal value differs from the maximal one almost ten times – 8,53–85,08 μg/ml. The mean of the leptin/adiponectin ratio is 0,85±0,68 (min-max 0,06–2,85). The adiponectin/BMI ratio is also characterized by wide limits – 0,27–4,29, the mean of this index is 0,93±0,67.

We determined a statistic-significant reverse correlation between the leptin and adiponectin concentrations – correlation coefficient $r$ = -0,30 ($p<0,05$).

We assessed the relation between the **adipokines metabolism parameters and BMI** in the women (table 27). For this assessment, we divided the researched into three groups according to their classification interval of BMI: norm (BMI<24,99), overweight (BMI 25,0–29,99) and obesity (BMI >30,0).

**Table 27**: BMI and women's leptin and adiponectin concentrations, leptin/adiponectin ratio and adiponectin/ BMI ratio

| | BMI | <24,99 | 25,0–29,99 | >30,0 |
|---|---|---|---|---|
| | N | 24 | 18 | 18 |
| Leptin, ng/ml | M±SD | 9,9±4,95 | 14,16±5,08 | 20,41±8,29 |
| | Min-max | 2,4–18,4 | 5,5–23,0 | 3,3–32,1 |
| | p | **0,01** | | **0,01** |
| | | **<0,001** | | |
| Adiponectin, μg/ml | M±SD | 28,12±16,53 | 17,93±6,37 | 23,89±15,75 |
| | Min-max | 11,48–85,08 | 8,53–29,84 | 9,43–55,89 |
| | p | **0,01** | | 0,15 |
| | | 0,41 | | |
| Leptin/adiponectin | M±SD | 0,50±0,44 | 0,94±0,57 | 1,24±0,82 |
| | Min-max | 0,09–1,52 | 0,23–2,27 | 0,06–2,85 |
| | p | **0,01** | | 0,21 |
| | | **0,002** | | |
| Adiponectin/BMI | M±SD | 1,29±0,85 | 0,67±0,24 | 0,72±0,48 |
| | Min-max | 0,49–4,29 | 0,29–1,19 | 0,27–1,75 |
| | p | **0,002** | | 0,68 |
| | | **0,01** | | |

We determined the leptin concentration progressively increases along with an increase in BMI. The adiponectin concentration in the women with normal BMI is statistic-significantly higher compared with the women with overweight. However, we did not find a statistic-significant difference in the adiponectin concentration in the other groups.

We determined the leptin/adiponectin ratio in the women with normal BMI is statistic-significantly lower than analogical indexes in the women with overweight or obese ones (p 0,01 and 0,002, respectively). We did not find a statistic-significant difference in the derived index between the women with overweight and obese ones. The adiponectin/BMI ratio is statistic-significantly higher in the women with normal BMI compared with analogical indexes in the women with overweight or obese ones (p 0,002 and 0,01, respectively). We did not find a statistic-significant difference in the adiponectin/BMI ratio between the women with overweight and obese ones like in the assessment of the leptin/adiponectin ratio (p=0,68).

We assessed the correlative ratio between the adipokines concentrations and the body mass and BMI. We determined a statistic-significant direct correlation between the leptin concentration and the body mass and BMI – the correlation coefficients were 0,66 ($p<0,01$) and 0,64 ($p<0,01$), respectively. The adiponectin concentration did not correlate statistic-significantly with the body mass or BMI – the correlation coefficients were -0,22 and -0,21, respectively.

We assessed the correlative ratio between the adipokines concentration and the changes in the body mass and BMI within 20 years. We found a statistic-significant direct correlation between the leptin concentration and an augment in the body mass and BMI – the correlation coefficient were 0,42 ($p<0,001$) and 0,40 ($p<0,001$), respectively. The adiponectin correlation is insignificant, *r* is -0,15 and -0,16, respectively.

We assessed the **correlation ratio between the adipokines concentrations and the adipose tissue and topographic parameters** (table 28).

**Table 28:** Correlation coefficients of the adipokines concentrations and anthropometric parameters

| | Leptin | Adiponectin |
|---|---|---|
| Passive body mass, percent | 0,38** | -0,24 |
| Passive body mass, kg | 0,46** | -0,26 * |
| Amount of eight skin folds | 0,49** | -0,25 * |
| Amount of torsio skin folds | -0,09 | -0,12 |
| Amount of limb skin folds | 0,61** | -0,19 |
| Ratio between the amount of torsiot skin folds and amount of limb skin folds | -0,57** | 0,24 |
| Amount of skin folds of the upper part of body | 0,46** | -0,27 * |
| Amount of skin folds of the lower part of body | 0,45** | -0,17 |
| Ratio between the amount of skin folds of the upper part of body and the amount of skin folds of the lower part of body | 0,34** | -0,30 * |

*) $p<0,05$; **) $p<0,01$.

We found the leptin concentration is statistic-significantly positively correlated with the amount of the passive body mass, amount of all eight skin folds, amounts of limb skin folds, skin folds of the upper and lower part of the body, ratio between the amounts of skin folds of the upper and lower part of the body; it is statistic-significantly negatively correlated with the ratio between the amounts of torsio and limb skin folds. In the case of the adiponectin concentration, we found less statistic-significant correlations. The concentration of this adiponectin is statistic-significantly negatively correlated with the absolute amount of the passive body mass, amount of eight skin folds, amount of skin folds of the upper body part and ratio between the amount of skin folds of the upper part of the body and the amount of skin folds of the lower part of the body. The adipokines correlation coefficients coincide with a lower level of significance than the leptin correlation coefficients.

We assessed the **ratio between the adipokines metabolism parameters and MS** (table 29).

**Table 29**: Leptin and adiponectin concentrations in MS (+) and MS (-) women, leptin/adiponectin ratio and adiponectin/BMI ratio

| | | MS (+) | MS (-) |
|---|---|---|---|
| | N | 22 | 38 |
| Leptin, ng/ml | M±SD | 18,97±7,38 | 11,65±6,13 |
| | Min-max | 3,30–32,10 | 2,40–29,70 |
| | p | **<0,001** | |
| Adiponectin, μg/ml | M±SD | 23,05±14,66 | 24,39±14,28 |
| | Min-max | 8,53–55,89 | 8,98–85,08 |
| | p | 0,73 | |
| Leptin/adiponectin | M±SD | 1,15±0,75 | 0,67±0,57 |
| | Min-max | 0,06–2,85 | 0,09–2,41 |
| | p | **0,01** | |
| Adiponectin/BMI | M±SD | 0,73±0,44 | 1,05±0,75 |
| | Min-max | 0,28–17,48 | 0,27–4,29 |
| | p | **0,04** | |

The leptin concentration in MS (+) women is statistic-significantly higher (<0,001) than the analogical parameter in the healthy women and exceeds the physiological norm limits. We did not find any significant differences in the adiponectin concentration between the groups.

We assessed the **ratio between the adipokines metabolism parameters and menopause** (table 30). For this assessment, we divided the researched into two groups – the women who had had their last menstruations a year or a longer time ago (hereinafter – menopause (+)) and the women with regular menstruation cycles or who had had their last menstruations less than a year ago (hereinafter – menopause (-)).

**Table 30**: Leptin and adiponectin concentrations in women, leptin/adiponectin ratio and adiponectin/BMI ratio and menopause

| | | Menopause (+) | Menopause (-) |
|---|---|---|---|
| | N | 19 | 41 |
| Leptin, ng/ml | M±SD | 17,7±7,3 | 12,8±7,1 |
| | Min-max | 7,6–32,1 | 2,4–32,1 |
| | p | **0,019** | |
| Adiponectin, μg/ml | M±SD | 24,30±16,93 | 23,71±13,15 |
| | Min-max | 8,98–85,08 | 8,53–59,63 |
| | p | 0,89 | |
| Leptin/adiponectin | M±SD | 0,75±0,62 | 1,05±0,76 |
| | Min-max | 0,06–2,41 | 0,09–2,85 |
| | p | 0,14 | |
| Adiponectin/BMI | M±SD | 0,93±0,91 | 0,93±0,54 |
| | Min-max | 0,27–4,29 | 0,29–2,80 |
| | p | 0,99 | |

According to our data, the leptin concentration after menopause is 17,7 ng/ml (SD=7,3, min-max 7,6–32,1) and it is statistic-significantly higher (p=0,019) than an analogical parameter before menopause– 12,8 ng/ml (SD=7,1, min-max 2,4–32,1). The mean of the leptin concentration exceeds the physiological norm limits in the women after menopause. We did not find any statistic-significant differences in the other indexes between the groups.

# 8. RESULT DISCUSSION

## 8.1 Long-term changes in the women's body

### *8.1.1 Changes in anthropometric parameters in researched women within twenty years*

Even 76,7 percent women had a physiologic normal body mass and BMI during the first research. 20 years later the body mass increased for most women (91,7 percent) and the body mass decreased for only 5 women (8,3 percent). BMI is a derived index defining the human body mass and height ratio, thus, increased body mass indexes and unchanged height indexes had an influence on the changes in BMI, too. According to our data, the statistic average BMI jumped from 22,99 to 27,17. It shows the women jumped

from the physiological norm interval of BMI (BMI < 24,99) to the interval of overweight (BMI = 25,00–29,99).

Our data about the changes in the women's body mass and BMI fully coincides with the data by other authors [97, 98–102, 105]. It is indicated in the literature women's body mass can increase by about 0,5 kg a year during perimenopause [121]. It is related with a slowdown in metabolism, remained bad nutritional habits, insufficient physical activity and development of resistance to insulin [121, 125, 128]. There are also other reasons – changes in the growth hormone, leptin, galanin, ghrelin and neuropeptide Y concentrations [130, 131].

When assessing the changes in the thickness of skin folds within 20 years, we determined only the chest skin fold thickened statistic-significantly and the chin, subscapular and biceps skin folds did not change statistically, the thickness of four other skin folds even decreased statistic-significantly. When assessing the relative part of separate skin folds in the total adipose tissue mass, we determined the part of the chin, subscapular, chest and biceps skin folds increased and the femoral and calf part decreased. The thickness of the chin, subscapular and biceps skin folds in the absolute numbers (mm) did not change statistic-significantly within 20 years; however, the relative part of these skin folds from the total amount of the skin fold parameters largely increased. Meanwhile, the thickness of the abdominal and triceps skin folds in the absolute numbers (mm) changed statistic-significantly, but these changes did not have a bigger influence on their percentage from the total amount of the skin fold parameters. Only a statistic-significant decrease in the thickness of the femoral and calf skin folds in the absolute numbers significantly correlates with a decrease in the percentage of these skin folds.

The total amount of the subcutaneous adipose tissue expressed in the amount of the thickness of all skin folds decreased statistic-significantly within 20 years. We detected the subcutaneous adipose tissue of the lower part of the body and limbs decreased significantly during the researched period. Only the amount of the subcutaneous adipose tissue in the upper part of the torsio increased significantly and this increase influenced the fact the total amount of the upper part of the body and the amount of the subcutaneous adipose tissue of the waist did not change statistically. According to our data, the total decrease in the amount of the subcutaneous adipose

tissue is influenced by a decrease in the amount of the subcutaneous adipose tissue of the lower part of the body and limbs.

When assessing the interrelations between the amount of separate skin folds, we determined there was a bigger amount of the adipose tissue in the upper part of the body than in the lower one 20 years later and the ratio between the adipose tissue dimensions in the torsio and limbs increases „to the benefit of torsio“. Therefore, it is possible to state there is a tendency of centralization of the subcutaneous adipose tissue when ageing.

When assessing the passive body mass parameters, we determined the relative amount of the passive body mass reliably decreased during the researched period. It is to note an analogical phenomenon was detected by Lithuanian researchers who compared the amount of the subcutaneous adipose tissue in pregnant women in 1986–1987 and 2003–2005 and wrote the pregnant women who were researched in 2003–2005 had a lower amount of the subcutaneous adipose tissue compared with the women researched in 1986–1987 [11].

However, the changes in the total body mass are both influenced by the changes in the subcutaneous adipose tissue and in the visceral mass. As the amount of the subcutaneous adipose tissue in the abdominal region decreased and the abdominal circumference increased statistic-significantly in the researched women, it can be logically state the visceral mass largely thrived within 20 years. A quantitative increase in the visceral mass „compensated“ a decrease in the subcutaneous adipose tissue and influenced the similarity in the average statistical parameters of the passive body mass expressed in the absolute numbers. This data of our research also coincides with the results by other researchers obtained by applying other research methods as they also prove the centralization of the adipose tissue [122–124].

We are also troubled by analogical tendencies of the changes in the younger women’s body structure described by Lithuanian and foreign authors [11, 12]. In the literature, a decrease in the subcutaneous adipose tissue in reproductive women, disappearance of the female-characteristic pear-shaped silhouette and changes in the body structure towards the shape of a cylinder are described. When assessing the data of our researches showing the development of metabolic-unfavourable centralization of the adipose tissue in reproductive women approaching to menopause, it is possible to

suspect these shifts will even be more obvious in the present generation of young women.

Thus, it is possible to think more comprehensive researches of the changes in the visceral mass (including the visceral adipose tissue) related with a woman's age are promising.

### *8.1.2 Metabolic changes in researched women within twenty years*

When assessing the metabolic changes for the researched women within 20 years, it is to note our data partially coincides with the literary data [159–161]. Like other authors, we determined the total increase in Ch and LDL cholesterol concentrations. The means of the total Ch and LDL cholesterol concentrations exceed even more liberal recommended limits [170].

The changes in the HDL cholesterol concentration and AC for which calculation the HDL cholesterol concentration parameters is used are not statistic-reliable in our researched group, but the tendencies of changes coincide with those indicated in the literature. Our data about the changes in the Tg concentration and derived parameters for which calculation the Tg concentration parameter is used, i.e., the ratio between the Tg and HDL cholesterol concentrations, does not coincide with the literary data. The Tg concentration and the ratio between the Tg and HDL cholesterol concentrations decreased statistic-significantly in the researched group, and it is indicated in the literature these lipid metabolism changes increased increase during perimenopause [159–161]. We think this discrepancy of the data received by us can be related with an increase in the Tg concentration starting for some researched women in early pregnancy which is described by other authors [11, 12, 116].

Within 20 years, the glucose concentration increased statistic-significantly. The mean of the glucose concentration in the researched women approaches to the values of the diagnostic criterion of MS indicated in TDF 2005 and AHA 2009 methodologies and the maximal values of these parameter exceed the physiological norm limits – the mean is 5,26 mmol/l (SD=0,72, min-max 1,93–6,64) [178, 203]. An increase in the women's glucose concentration described by us coincides with the data by other authors [160].

When assessing the resistance to insulin in the researched women, we found even one fifth of the researched women had increased resistance to insulin. It is indicated in

the literature the resistance to insulin is diagnosed for about 16 percent women after menopause [167]. Thus, our data is close to the data by other authors.

Thus, we determined the metabolic changes which are unfavourable for the women of the researched group – dyslipidaemia of proatherogenic type and increased glucose concentration and increased resistance to insulin.

## 8.2 Peculiarities of anthropometric and metabolic changes in healthy and metabolic syndrome women during pregnancy and within twenty years

We will remind all the women of the researched group were healthy in early pregnancy. Only 20 years later they were divided into two groups – MS (+) and MS (-). However, it was possible to notice inequalities of the amount of the subcutaneous adipose tissue and its distribution in these groups already during pregnancy. MS (+) women have a bigger body mass and higher BMI and passive body mass already in early pregnancy, the amount of measured skin folds is higher. Almost all the measured skin folds (except the calf skin fold) are much bigger in these women compared with the healthy ones. Thus, they accumulate more subcutaneous adipose tissue. A bigger accumulated visceral mass is shown by a bigger abdominal circumference in these women. The most obvious statistic-significant differences were found when assessing the abdominal and chest circumference, parameters of thickness of subscapular, chest and abdominal skin folds and the amounts of torsio skin folds and skin folds of the upper part of the body. The subcutaneous adipose tissue in MS (+) women in early pregnancy keeps the proportions of distribution which are similar to those in healthy women despite a locally bigger amount. However, it is already possible to notice a tendency of accumulation of the subcutaneous adipose tissue in the waist region and the region of the upper part of the body. It shows the tendency of centralization of the adipose tissue in MS (+) women which was already present in early pregnancy.

There are no differences in the metabolic parameters – lipid and glucose metabolism ones –in early pregnancy. According to the data by other authors, there is a relation between hyperglycaemia during pregnancy and risk of the development of MS [156, 157].

Thus, the differences in the body structure dominated in our researched group between MS (-) and MS (+) in early pregnancy. Our data mostly reflects the differences

in the amount of the adipose tissue between the groups of women and the tendency of centralization of the adipose tissue in MS (+) women. During pregnancy, the amount of the subcutaneous adipose tissue increased in MS (+) and MS (-). Common features of changes: increasing subscapular, chest and femoral skin folds. Thus, the localization of a growth in the adipose tissue reminded of the shape of a sandglass or a pear. The topographic features of the subcutaneous adipose tissue characteristic to females became obvious.

We also detected the peculiarities of changes distinguishing MS (+) and MS (-) women. For MS (+) women, the amount of the adipose tissue also increased in other regions – the triceps and biceps skin folds and calf fold increased for them during pregnancy on the contrary to the healthy ones. Thus, a growth in the subcutaneous adipose tissue for those pregnant women who will have MS in the future is characterized by the tendency of decentralization.

We think this peripheral growth in the subcutaneous adipose tissue could be useful when prognosticating a risk of the development of MS.

We found two anthropometric indicators which could help to prognosticate a long-time risk of the development of MS. One of the body markers determined by us – the relative change in the triceps skin fold – reflects the decentralization of the subcutaneous adipose tissue above. A risk of MS 20 years later is almost 5 times higher for the women whose subcutaneous adipose tissue increases in the triceps region during pregnancy compared with those for who this skin fold decreases.

The second body marker – the ratio between the absolute growth in the passive body mass during pregnancy and the neonate's birth mass. The data of our research shows a risk of MS 20 years later is more than 20 times higher for the women who put on more than 1,29 kg of the passive body mass per each kilo of their foetus during pregnancy compared with those who put on less weight.

These results of the research allow expecting the assessment of the body markers proposed by us can be a simple non-invasive research enabling assessing an individual long-time risk of MS for every pregnant woman. Therefore, more comprehensive analogical follow-ups should be promising.

In our opinion, the derived parameters above reflect the adaptation of mechanisms of the pregnant woman's organism to the new biological task – to carry, give birth to a

baby and nurse him/her. In spite of a bigger amount of the absolute adipose tissue accumulated by MS (+) women in early pregnancy (both the subcutaneous adipose tissue and the visceral mass), their organism bears a bigger load and higher energy expenditures during pregnancy and accumulates more passive body mass compared with the healthy women's organism. These results of our research make think about a different "quality" of the adipose tissue in MS (-) and MS (+) women – different properties of the adipose tissue and unequal possibilities to regulate metabolism. It would coincide with an interesting concept of adiposopathy proposed by H. E. Bays [33, 36–42]. MS (+) women can contain namely this "faulty" or "inferior" adipose tissue which qualitative defects may be compensated with a bigger amount. Meanwhile, the pregnant woman's organism must create maximally favourable conditions for the foetus's development during pregnancy. These conditions involve certain metabolism homeostasis, concentrations of constructional, energetic and other materials and their expression in the tissues and their retention in the physiological norm limits. According to the literary data, the metabolic parameters change during pregnancy – there is a growth in the lipid metabolism parameters and glucose concentration in serum and a change in the extent of the hormone production [139, 141, 150, 152]. The metabolic changes during pregnancy depend on the pregnant woman's body structure [116, 153]. The adipose tissue forms a buffer medium which actively participates in metabolism and must compensate deviations of the metabolism components beyond the physiological norm limits. In order to ensure this aim, the amount of the adipose tissue accumulated in the woman's organism can be insufficient. In case the adipose tissue in the pregnant woman is healthy and its metabolism possibilities are full-fledged, a growth in her body mass during pregnancy should coincide with the norms recommended in the literature [115, 117]. A part of this growth in the pregnant woman's body mass will also consist of a growth in the passive body mass in the pregnant woman which is proportional to the needs of the developing foetus's organism.

In the case of dysfunction of the adipose tissue, the pregnant woman's organism must compensate it. The accumulation of a bigger amount of the passive body mass which is proportional to the needs of the developing foetus's organism and decentralization of the adipose tissue which we described according to the data of our research may be one of such compensational mechanisms.

20 years later the reproductive age gradually ends for all women. They also lose a part of the subcutaneous adipose tissue – there is a decrease in the total amount of the subcutaneous adipose tissue. There is a change in the topography of the adipose tissue. The parameters of the thickness of the femoral skin fold largely decrease; there is an increase in all three derived relative indexes of the amounts of skin folds (upper part of the body and lower part of the body, torsio and limbs and upper part of the body and all eight skin folds). Thus, the features of distribution of the adipose tissue of female type are lost. These are common changes characteristic to age.

However, the differences in the anthropometric changes in MS (-) and MS (+) women are seen again. Within 20 years, the previous statistic-reliable difference in the thickness of the femoral skin fold between the groups disappears and a new statistic-significant difference in the thickness of the calf skin fold between the groups appears – there is more subcutaneous adipose tissue in this region in MS (+) women. When analyzing the changes in the amounts of skin folds of the upper part of the body and waist skin folds, the following tendency is noticed: within 20 years the amounts of skin folds of these body regions increase in MS (+) women compared with the values of these indexes in early pregnancy; analogical indexes decrease in healthy women.

When analyzing the abdominal circumference parameters, we noticed the abdominal circumference largely increased within 20 years in MS (+) women and did not change in MS (-) women. It shows an increase in the amount of the visceral mass in MS (+) women.

Thus, the shape of a sandglass or a pear determined by the subcutaneous adipose tissue disappears in healthy women when ageing and the body obtains the shape of a cylinder. In MS (+) women, the adipose tissue starts dominating in the upper part of the body along with a decrease in the subcutaneous adipose tissue in the lower part of the body and limbs; these women’s body obtains the shape of an upturned pear and there is an increase in the visceral mass.

Along with a decrease in the amount of the adipose tissue, there is also a decrease in the volume of the medium buffering deviations of the metabolism components; therefore, there is a decrease in the compensational and homeostasis-retention possibilities of the organism. Thus, at the end of the research we determined statistic-

significant unfavourable changes in most lipid metabolism parameters for the women – increase in the glucose, total Ch, LDL cholesterol concentrations AC and AIP.

If continuing the idea above about the dysfunction of the adipose tissue, it is also possible to logically explain the peculiarities of the metabolic parameters in MS (+) women – their glucose and Tg concentrations are higher than those in healthy women, resistance to insulin is higher and atherogenic properties of the blood serum are more obvious.

### 8.3 Peculiarities of serum leptin and adiponectin concentrations in women's blood under physiological and pathological conditions

We found the leptin concentration coincided with the physiological norm limits in the researched women and the minimal and maximal values were quite wide. We determined the adiponectin concentration had wide limits. The adiponectin concentration limits indicated in the literature are also quite wide – 3,62–31,82 μg/ml [32, 107–109].

According to the data of our researches, we determined the values of the derived parameters of the adipokines metabolism are close to those indicated in the literature. The following values of the leptin/adiponectin ratio are indicated in the literature – 0,42–0,79 μg/ml in the case of a normal body mass and 1,2–2,29 μg/ml in the case of obesity [107, 108].

We determined a statistic-significant reverse correlation between the leptin and adiponectin concentrations – correlation coefficient $r$ = -0,30 ($p<0,05$). These results also coincide with the literary data [49].

When assessing the relation of the adipokines metabolism parameters with women's BMI, we found the most obvious differences in the case of leptin – the leptin concentration increases in respect of each classification interval of BMI. In the case of the adiponectin concentration, the differences between different groups of the classification intervals of BMI were least expressed. A statistic-reliable difference was only detected between the women with normal BMI and overweight BMI. The Lithuanian authors who had researched 149 patients of the both sexes were not able to determine a statistic-significant difference in the adiponectin concentration between the patients whose BMI <30 and >30 [32]. We assessed the concentration of adiponectin by dividing the researched into three classification intervals of BMI and found some statistic-significant differences in the adiponectin concentration.

Literary sources state the leptin concentration is statistic-significantly directly correlated with the body mass and BMI [66, 94, 100]. Thus, our data coincides with that published in the literature.

According to the literary data, the adiponectin concentration and body mass and BMI are statistic-significantly reversely correlated [112, 100]. Other authors only determined a statistic-significant negative correlation between the adiponectin concentration and BMI in the group of healthy persons, but they did not find such kind of correlation in patients with DM, glucose tolerance disorder or CHD [32, 89]. The data of our research revealed a statistic-insignificant tendency of correlation between these parameters; however, it is close to statistic significance and analogical to that described in the literature.

According to the literary data, the leptin/adiponectin ratio also positively correlates with BMI, the derived parameters can reflect the resistance to insulin, tendency to have MS and the amount of the visceral adipose tissue more sensitively than the adipokines concentration alone [71, 86 91, 92]. According to the data of our research, as we divided the researched women according to their BMI, the differences in the derived indexes between the groups were more obvious than the differences in the adiponectin concentration but less obvious than the differences in the leptin concentration. It is interesting the differences in the derived indexes, especially adiponectin/BMI ratio, were more obvious than only the differences in the adipokines concentration between the groups after dividing the researched according to the change in the classification interval of BMI.

When assessing the correlative ratio between the adipokines concentrations and the parameters reflecting the topography of the adipose tissue, we found statistic-significant correlative ratios in the case of the both adipokines. However, the leptin concentration has a stronger relation with the anthropometric parameters compared with the adipokines concentration. It is indicated in the literature the adipokines concentration correlates with various body structure parameters: the adiponectin concentration correlates with the trunk fat-leg fat ratio and the amount of the passive body mass statistic-significantly; WHR; leptin concentrations – with the amount of the passive body mass [32, 88, 100, 102, 104]. Thus, the data of our research about the adipokines concentration and passive body mass coincides with the literary data. Besides, we found

other statistic-significant correlations between these adipokines concentrations and body structure parameters.

When assessing the ratio between the adipokines metabolism parameters and MS, we detected statistic-significant differences in the leptin concentration and derived indexes; we did not find any differences in the adipokines concentration between MS (+) and MS (-) women. It is indicated in the literature the leptin concentration is higher in the case of MS compared with the healthy people's parameters and the adiponectin concentration is lower [66, 87, 172]. Some researchers indicate the leptin/adiponectin ratio significantly correlates with the resistance to insulin and tendency to have MS; this ratio can be a marker of atherosclerotic changes in the walls of vessels assessed as a proper index for the metabolism control in the case of DM [106–108]. According to the data by other authors, the adiponectin/BMI ratio is good for observing the efficiency of treating DM of type II [112]. Thus, the data of our research partially coincides with the literary data. The data of our research shows the derived indexes reflect the peculiarities of metabolism in MS (+) women better than the adiponectin concentration parameters alone.

When assessing the relation between the researched women's adiponectin metabolism parameters and menopause, we found a statistic-reliably higher leptin concentration in women after menopause compared with those still having menstruation cycles. We did not find any other differences in the adipokines metabolism indexes between the groups. According to the literary data, the leptin concentration can be higher or unchanged during perimenopause compared with this parameter in fertile women. In the authors' opinion, in depends on the woman's BMI. The adiponectin concentration decreases or does not change during perimenopause [93, 94]. Thus, the data of our research coincides with that published in the literature.

The research data show the leptin concentration changes after menopause and the adiponectin concentration does not. The increase in the leptin concentration is an unfavourable factor. Along with the tendencies of the changes in the women's body structure above (increased body mass and BMI, distribution of the adipose tissue towards centralization), it reflects unfavourable metabolic changes in the women's organism – a tendency of the development of resistance to insulin, MS and atherogenic changes.

## 9. CONCLUSIONS

1. The following long-term changes in the anthropometric parameters were determined for the researched women:

1.1 The women's body mass and BMI largely increased within twenty years.

1.2 Both the absolute adipose tissue mass and its topography changed within twenty years. The tendency of a decrease in the amount of the subcutaneous adipose tissue and centralization was determined. Increased abdominal circumference shows increased amount of the visceral mass.

2. The following unfavourable long-term changes in the women's metabolic parameters were determined:

2.1 The lipid metabolism parameters obtain a proatherogenic profile in the researched women.

2.2 The glucose concentration statistic-significantly increased in the researched women within twenty years.

2.3 There is an obvious growth in the women's body mass and change in the classification interval of BMI from the norm to obesity is related with the frequency of HOMA-IR indexes above the physiological norm and the metabolic syndrome.

3. The following differences in the anthropometric parameters for metabolic syndrome and healthy women were determined:

3.1 The first body markers were already detected during pregnancy for the women who had the metabolic syndrome at the end of the research: their body mass and BMI was bigger in early pregnancy and they accumulated more passive body mass; during pregnancy, we found the tendency of decentralization of the subcutaneous adipose tissue for them.

3.2 At the end of the research, the adipose tissue started dominating in the upper part of the body in the metabolic syndrome women; these women's body obtained the shape of an upturned pear and there was an increase of the visceral mass.

4. The following peculiarities of metabolism were determined in the metabolic syndrome and healthy women:

4.1 There were no differences in the lipid and glucose metabolism parameters during pregnancy in the metabolic syndrome and healthy women.

4. Within twenty years after birth, some lipid metabolism parameters and the glucose concentration were higher in the metabolic syndrome women compared with those in the healthy women.

5. A statistic-reliable reverse interrelation between the leptin and adiponectin concentrations was determined. In the researched women, the relation between the adipokines metabolism parameters and the anthropometric parameters and their changes within 20 years and menopause and the metabolic syndrome was found.

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## 11. LIST OF PUBLICATIONS

1. J. Volochovič, G. Drąsutienė, V.Urbanavičius, Z. Kučinskienė. Adipokinai ir jų vaidmuo moters reprodukcinės sistemos funkcijai ir patologijai. Laboratorinė medicina, 2008; 3(39): 168-173.

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**Short information about author**

Jelena Volochovič was born in Šalčininkai on the 21st of May 1975.

In 2000 she graduated from the Faculty of Medicine of Cracow Jagellonian University. In 2000-2001 she studied at the resident practice of a medical doctor at Vilnius University, in 2001-2005 – at the resident practice of an obstetrician-gynaecologist at Vilnius University. In 2005-2010 she was a graduate of the Faculty of Medicine at Vilnius University.

In 2004 she trained at the Clinic of Obstetrics and Gynaecology of Lublin Medicine Academy. In 2004-2005 she worked as an assistant doctor in the obstetric-neonatal department at Centre branch of Vilnius University Hospital "Santariškių Klinikos". Since 2005, she has worked as an obstetrician-gynaecologist in the obstetric-neonatal department at Centre branch of Vilnius University Hospital "Santariškių Klinikos".