ORIGINAL ARTICLE

THE ROLE OF LEPTINRESISTANCE IN THE PATHOGENESIS OF OBESITY IN PREGNANT WOMEN

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ABSTRACT

The aim: To investigate the relationship between leptin resistance, lipid and carbohydrate metabolism, blood pressure in obese pregnant women.

Materials and methods: Under observation were 65 women (main group) with obesity (I degree -27 women, II degree - 24 women, III degree - 14 women) in the II trimester of pregnancy, who were hospitalized in the Department of Pathology of Pregnancy KNP «Maternity Clinical house №1 "in Lviv during 2017-2020 on preeclampsia of varying severity, which were sent for inpatient treatment by women's clinics. The control group consisted of 30 healthy pregnant women without obesity.

Results: Serum leptin in obese women was directly correlated with BMI ($r = 0.66$, $p<0.001$), body weight ($r = 0.29$, $p<0.05$), total cholesterol (cholesterol) ($r = 0, 37$, $p<0,009$), low density lipoproteins (LDL cholesterol) ($r = 0.33$, $p<0.05$) and inversely with high density particles (HDL cholesterol) ($r = -0.37$, $p<0.02$). Studies of carbohydrate metabolism indicate the following correlation coefficients of BMI with glucose level $r = 0.351$; $p<0,001$, BMI with the level of C-peptide $r = 0,450$; $p<0,001$, BMI with HOMA index $r = 0,1504$; $p = 0.036$. Inverse correlations of C-peptide were detected with the level of P ($r = -0.169$; $p = 0.025$).

Conclusions: The discovery of the relationship between leptin resistance, lipid and carbohydrate metabolism, blood pressure indicates the possibility of using signs of leptin resistance to prevent complications during pregnancy in the second trimester.

KEY WORDS: leptin, cholesterol, glucose, C-peptide, HOMA index

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INTRODUCTION

The problem of obesity is becoming increasingly important today and poses an economic, medical and social danger to human life, regardless of social or occupational distribution, place of residence, age or gender. Obesity is a chronic disease that manifests itself in pathological deposition of fat in the body and excessive weight gain. In different countries, about 10% of the health budget is spent on the treatment of obesity and related pathologies. Only 50% of the population of Ukraine has a normal weight. Instead, more than 22% are obese. According to statistics, the mortality rate of young people due to overweight is 12 times higher than for people with normal body weight.

Compared with 1960, the caloric content of food increased by 24-26%, probably due to increased consumption of refined carbohydrates, transgenic fats, sodium, potassium, fiber, non-compliance with water regime, physical activity. An important role in this is played by increased levels of stress hormones, mutations in signal receptors to insulin and leptin molecules, which are one of the causes of obesity. Other factors are hedonistic consumption of food, which brings pleasure, reduces stress levels, as well as genetic predisposition to obesity, which (according to the literature) accounts for 40-70% of all causes, sedentary lifestyle, smoking, psychosocial factors.

Table I. Characteristics of lipid metabolism of examined pregnant women, M+m (95% CI)

Indicator	Clinical group		p between groups by t-test
	Main group (n=65)	Control group (n=30)	
Cholesterol, mmol/l	5,58±0,10	5,15±0,17	0,014
Triglycerides, mmol/l	1,87±0,07	1,76±0,12	0,812
LDL, mmol/l	2,68±0,05	2,34±0,11	0,30
VLDL, ммоль/л	0, 468±0,21	0, 412±0,20	0,23
HDL, mmol/l	1,58±0,02	1,69±0,02	0,609
Atherogenicity index (AI)	2,43±0,06	2,07±0,10	0,004

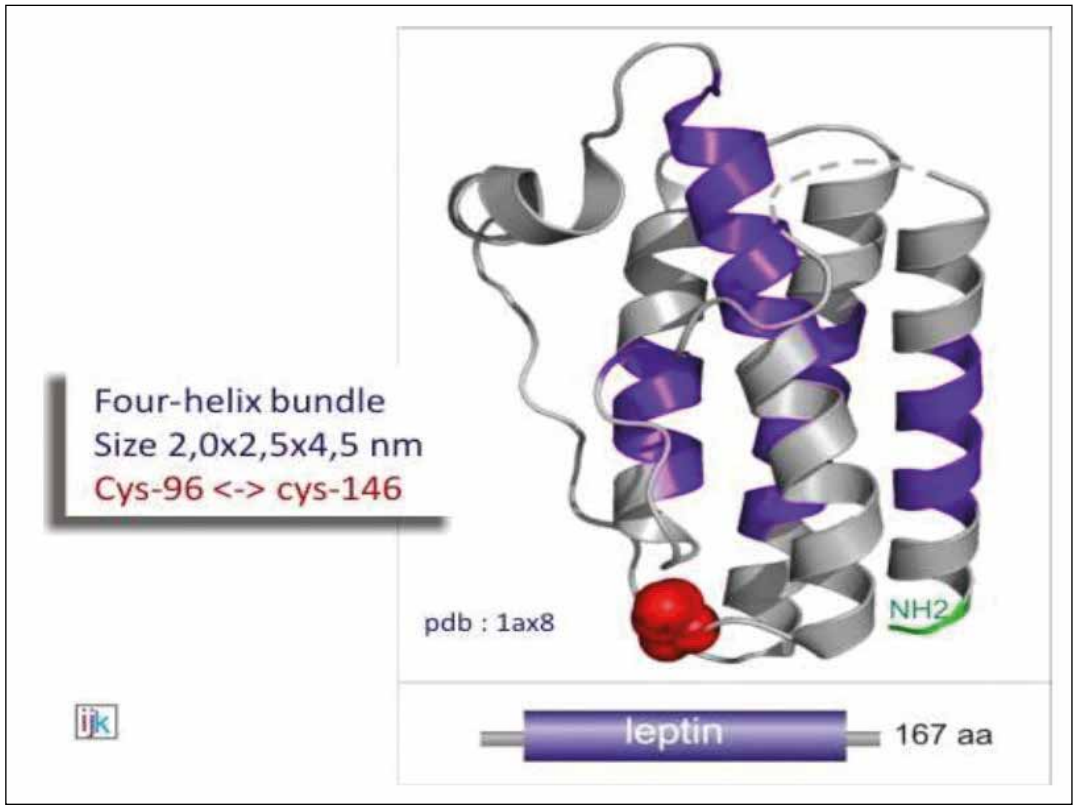

Fig.1. The structure of the leptin molecule.

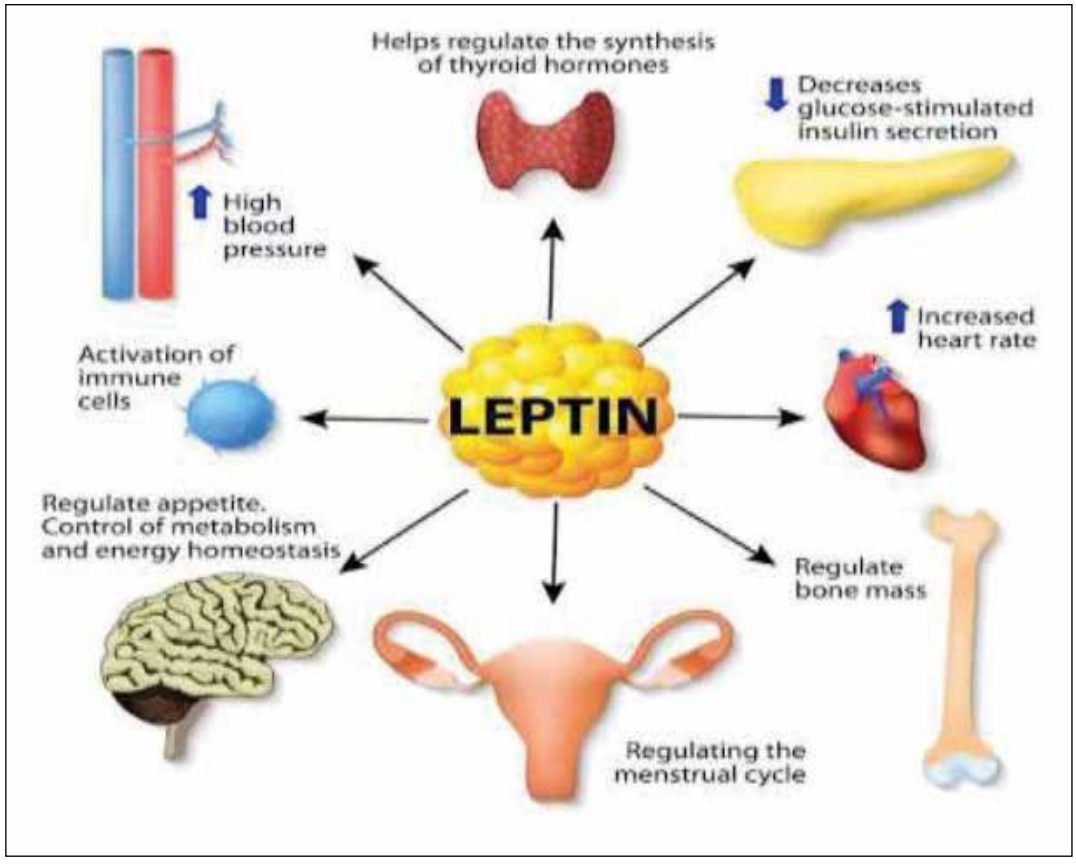

Fig.2. Main effects of leptin

Today, the theory of economical genotype remains relevant, the basis of which is hyperinsulinemia in conditions of increased food intake and, as a result, the emergence of excess body weight.

Recently, the role of adipose tissue, which is considered an endocrine and paracrine organ that produces a number of hormonally active substances - adipokines (adipose derived hormones), which cause disorders of carbohydrate

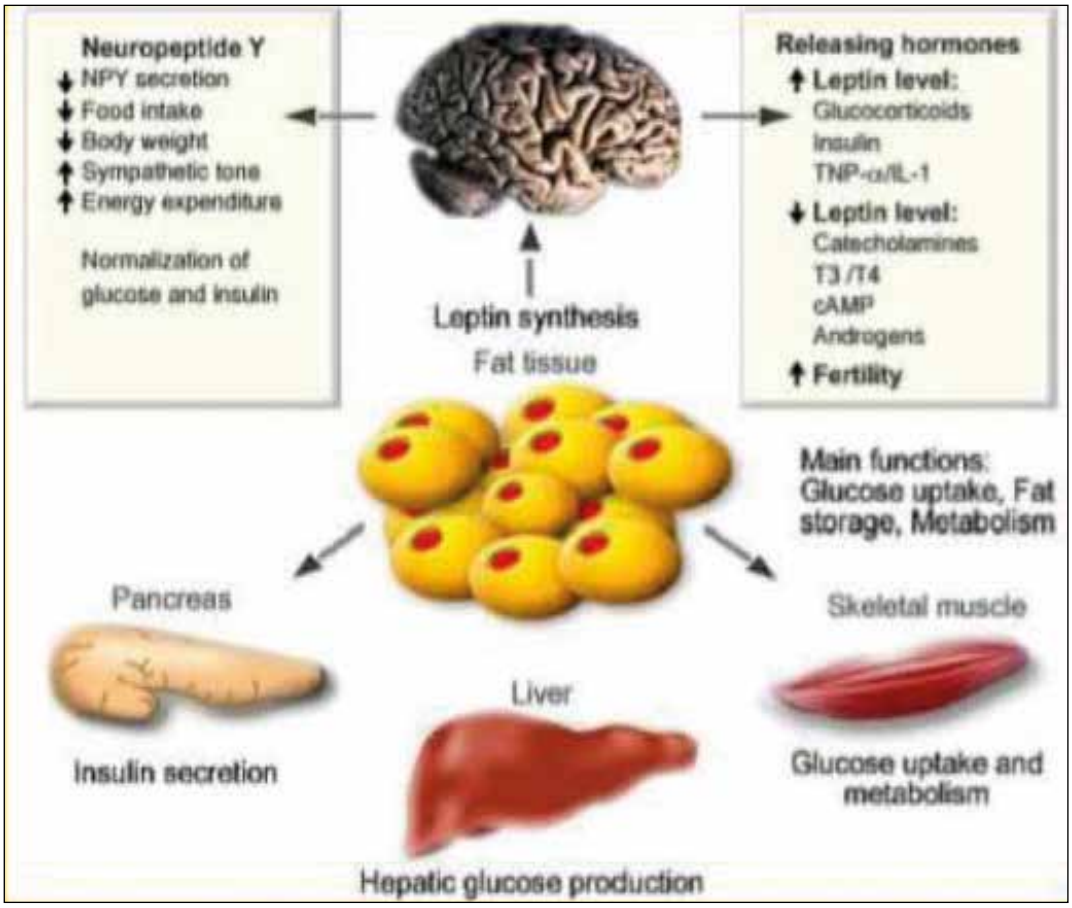

Fig. 3. Scheme of pathophysiology of lipid metabolism.

Table II. Characteristics of carbohydrate metabolism in women of the examined groups, M±m (95% CI)

Indicator	Clinical group		p between groups by t-test
	Main group (n=65)	Control group (n=30)	
Insulin, μOd / ml	10,54±0,35	10,86±0,41	0,05
Blood glucose, mmol/l	4,58±0,07	3,93±0,07	<0,001
C-peptide ng/ml	1,65±0,05	1,03±0,04	<0,001
Glycosylated hemoglobin,%	4,80*	4,80*	0,448**
HOMA index	2,02±0,06	1,90±0,04	0,041

Note: *- Data are presented in the form of Me [25%; 75%]; **- by U-criterion

Table III. Leptin levels and blood pressure in examined pregnant women, M±m (95% DI)

Indicator	Clinical group				p between groups by t-test
	Main group (n=65)			Control group (n=30)	
	I degree	II degree	III degree		
Leptin ng / ml	31,16±0,04	39,86±0,05	48,59±0,03	17,12±0,03	<0,05
SBP mm Hg	143,0±1,2	152,3±1,4	163,4±4,3	135,8±1,1	<0,001
DBP mm Hg	80,3±1,8	86,5±2,3	90,4±2,1	85,6±2,1	<0,001

and lipid metabolism, regulate inflammation and immune homeostasis, has been significantly revised [1-8]. The most famous of these is leptin [8].

The hormone leptin is a low molecular weight α-helix protein (16 kDa, 167 amino acids), which by its crystal structure belongs to cytokines (Fig.1). Leptin molecules circulate in the blood in both free and protein-bound form.

Leptin plays an important role in the regulation of metabolism and functions of the neuroendocrine system, including the pituitary gland, hypothalamus, adrenal glands, immune system. (Fig.2).

Leptin, which is produced by adipocytes, interacts with the long isoform of the leptin receptor LRb in the nuclei of the hypothalamus, activating metabolism, sympathetic

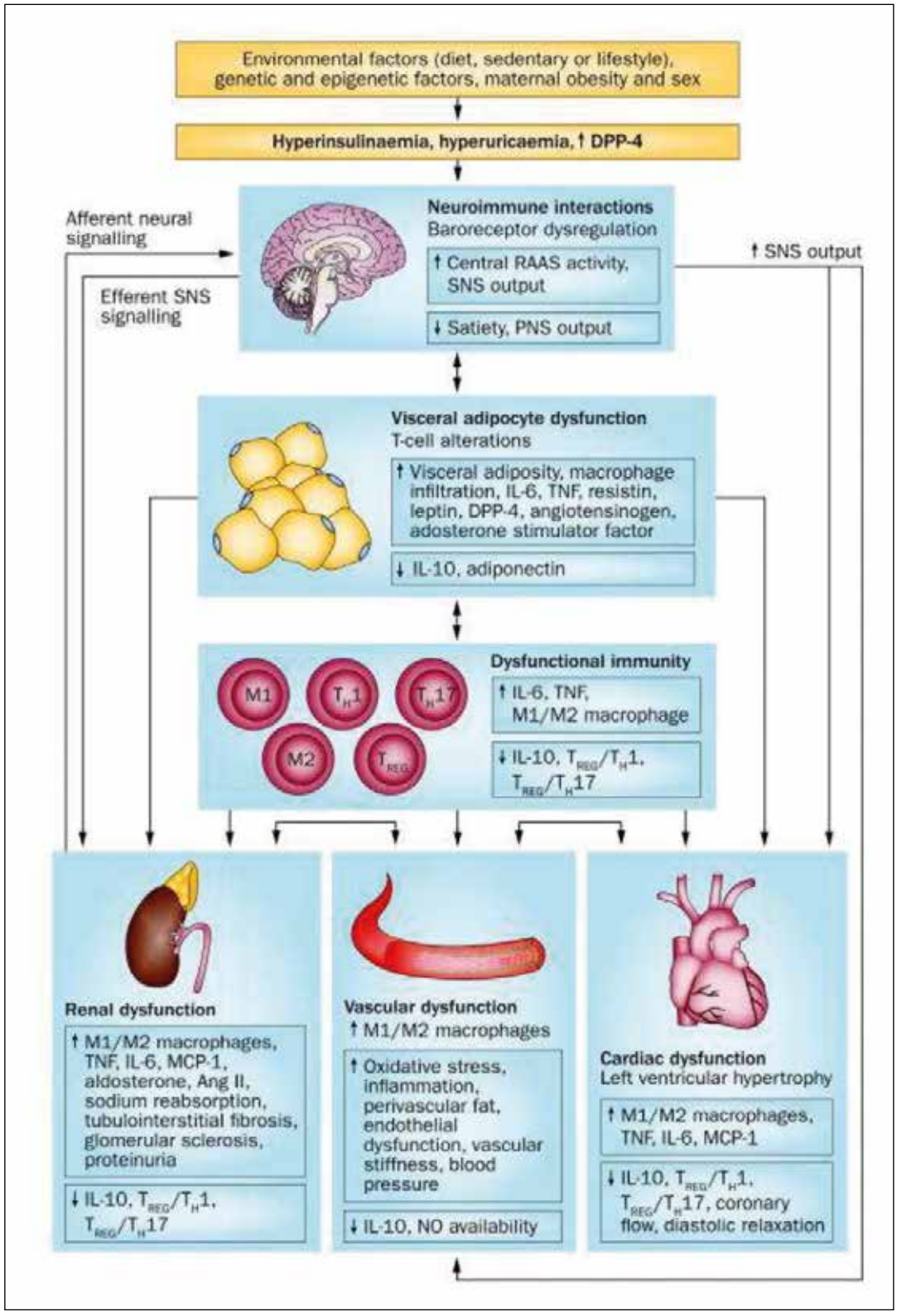

Fig.4. Pathogenesis of arterial hypertension in obesity.

nervous system tone, thyroid function, synthesis of sex hormones and growth hormones. Leptin enhances the immune response by activating LRb on T cells, and increases insulin sensitivity and regulates body weight by inhibiting satiety.

In recent years, there have been experimental data on the involvement of leptin in the induction and regulation of chronic inflammatory processes and degenerative diseases, including autoimmune pathologies, type 2 diabetes [1]. In humans, leptin is synthesized by cells of white and brown adipose tissue, skeletal muscle, stomach and placenta. Subcutaneous adipocytes produce 2.5 times more leptin than visceral fat. Leptin acts on the centers of hunger and satiety in the hypothalamus, is involved in the regulation of energy homeostasis and controls body weight by reduc-

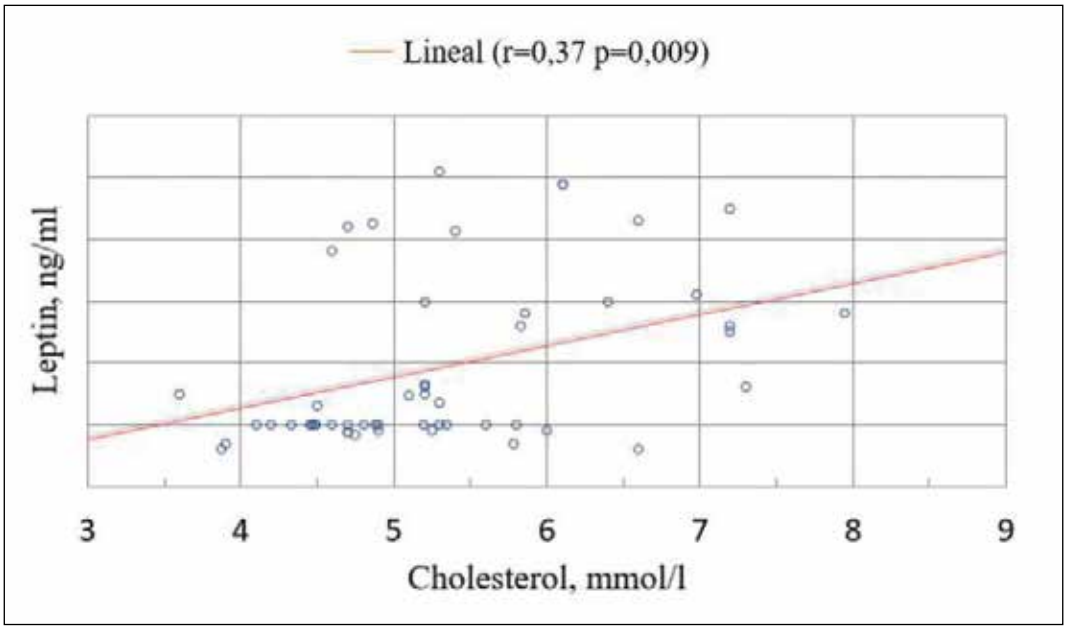

Fig.5. Dependence of leptin level on cholesterol concentration.

ing biosynthesis and the release of neuropeptide Y, which causes a feeling of hunger. Leptin secretion is not constant: its peak is observed in the afternoon, the minimum level after midnight. Obesity causes compensatory resistance of the hypothalamus to the central action of leptin, which subsequently leads to hyperleptinemia by the mechanism of negative feedback. It is believed that leptin is a link between adipocytes and β-cells of the pancreas and stimulates insulin secretion by reducing insulin sensitivity. There was a direct relationship between leptin levels and the degree of insulin resistance, taking into account changes in adipose tissue volume in postmenopausal women. In both in vitro and in vivo studies, leptin has been shown to function as a growth factor, stimulating angiogenesis, hematopoietic cell proliferation, and pancreatic β-cells. In addition, by suppressing the synthesis of neuropeptide Y in the hypothalamus, leptin stimulates the secretion of growth hormone in the pituitary gland. It is believed that leptin levels are a signal marker of sufficient accumulation of adipose tissue [2]. This process is necessary for puberty, regular menstrual cycles and provides the ability to reproduce. In healthy children in the prepubertal period, leptin levels increase in parallel with weight gain, reaching a maximum during puberty. Thus, leptin is considered as one of the triggering factors that initiate puberty [3,4].

Population studies in a number of European countries and the United States in the period 1990-2005 found an increase in the proportion of women of childbearing age with obesity from 9.9% to 16%. Adipose tissue is an endocrine organ that produces adipokines – leptin and adiponectin, which regulate fat metabolism and the risk of tumors, including breast cancer, endometrium [5,6]. As a rule, the level of leptin in the blood of women with a high (>25) body mass index is also elevated. This leads to impaired ovarian secretion of gonadotropic hormone and steroids, abnormal ovarian maturation, ovulation disorders and defects in endometrial development, as well as defects in implantation and early embryogenesis, which adversely affect female fertility. Normally, the concentration of free leptin in the serum reaches a maximum in the last luteal phase and decreases in the early follicular phase. In obesity, this cyclic content of leptin, as well as estradiol, is often disrupted and affects the ovulation process. In the luteal phase of the cycle, leptin stimulates apoptosis, as well as the synthesis of prostaglandin F2α, activating the regression of the corpus luteum. Leptin concentration balance provides luteolysis and apoptosis of corpus luteum cells in the absence of pregnancy. However, during fertilization and implantation of the egg, this balance is important for the normal development of the corpus luteum. In the culture of luteinized granulosa cells obtained from women participating in the IVF program, excess leptin concentration suppressed the expression of estradiol by these cells. It is noted that the violation of the normal balance of leptin adversely affects ovarian function, reducing the secretion of estradiol in granulosa cells. In addition, leptin can regulate ovulation by stimulating proteolysis and the release of follicle contents [7].

During pregnancy, the level of leptin in the blood rises, and after childbirth and abortion – falls. During pregnancy, leptin is additionally produced in the placenta and amniotic membranes, as well as in uterine tissues, inhibiting the contraction of uterine smooth muscle [3,8]. Recently, there are data on the pleiotropic effect of leptin on reproduction and pregnancy. In particular, the expression of leptin in the placenta enhances the proliferation and differentiation of trophoblast cells. Leptin production in the placenta is regulated by 17β-estradiol, which plays a key role in blastocyte implantation, in trophoblast differentiation and invasion, as well as in the regulation of uterine vascular growth and in the activation of protein kinase signaling pathways [9].

With obesity and abnormal serum leptin concentrations, there are usually pathological changes in the endometrium

and a low probability of implantation of a fertilized egg in the uterus, as well as the usual miscarriage [9,10]. Leptin receptors are found in the integumentary and glandular epithelium of the endometrium, their interaction with leptin activates the proliferation of stroma cells and endometrial epithelium, which ensures successful implantation of the egg. There are data on the contribution of leptin in the pathogenesis of endometriosis by autocrine and paracrine regulation [11, 12]. A multivariate analysis of 2527 married childless women and a control group of married women with many children shows that with increasing weight they increase the risk of cycles without ovulation, and the risk of low fertility is statistically significant at a body mass index > 23.9 [13]. As a rule, hyperleptinemia and leptin resistance are observed in obesity. This resistance is caused by several reasons: disruption of the production of various isoforms of the leptin receptor, inactivation of leptin molecules due to binding to blood proteins, disruption of hormone transport across the blood-brain barrier and insulin resistance. Hyperinsulinemia and insulin resistance have been shown to be associated with high blood leptin levels, regardless of body mass index [14].

Leptin regulates a number of neuroendocrine functions. In particular, disruption of the interaction of leptin molecules with its receptor leads to hypothalamic amenorrhea. Binding of leptin molecules to the long leptin receptor isoform mediates signal transduction and stimulates the synthesis of neuropeptides in the hypothalamus, which play a key role in puberty and reproduction. Mutations in the *Lep* gene encoding leptin in humans have been described, leading to hypolectinemia and delayed pituitary gonadotropic function with the development of hypogonadism due to gonadotropin-releasing hormone (GnRH) deficiency. Mutation of the *Lep* gene associated with congenital leptin deficiency, moderate obesity and signs of hypogonadotropic hypogonadism. A rare mutation in exon 6 of the LepR gene (PZ16T) is also associated with early obesity, severe hyperphagia, hypogonadotropic hypogonadism, neuroendocrine and metabolic dysfunction [15, 16,17].

Leptin is not synthesized by ovarian cells, but its concentration in follicular fluid is close to the concentration in the blood. The effect of leptin on ovarian function is ambiguous and depends on the stage of puberty. Leptin has been found to affect the activity of steroidogenic enzymes and folliculogenesis.Using immunocytochemical methods, transcripts of Lep and LepR genes (mRNAs) encoding leptin and its receptors were detected in the ovaries of adult women and adolescents, as well as in the embryonic ovaries at 2-3 weeks of gestation. The expression of leptin and the long isoform of its receptor, as well as the corresponding mRNA, were detected in oocytes of primordial and more mature follicles, and the expression of leptin in – granulosa cells [18]. There are also data on the role of leptin in the development of polycystic ovaries.It has been shown that in patients with this syndrome, who reduced body weight to normal values, the menstrual cycle normalized, oligo- and anovulation were observed much less frequently, and the probability of pregnancy increased. This is due to the restoration of the balance of hormones that regulate the development of follicles and egg maturation [5]. Hyperleptinemia, which is associated with overweight and obesity, is considered a risk factor for chronic oligo- or anovulation, which is caused by both insulin resistance and leptin-dependent ovarian dysfunction [19] (Fig.3).

There are data in the literature on the role and importance of leptin in hypertension (AH) [4, 9, 6, 10], but they are not yet final. Thus, the determination of leptin in 123 patients with hypertension showed that with increasing its level there is not only a progressive increase in body mass index and waist circumference, but also systolic and diastolic blood pressure (BP), insulin and insulin resistance index HOMA [5]. Some researchers consider leptin to be one of the means of regulating blood pressure. Evidence of this is that leptin receptors are found in the cells of the adrenal medulla, which may indicate the regulation of leptin synthesis of catecholamine vasopressors. At the same time, high levels of catecholamines reduce leptin secretion by activating beta-adrenergic receptors (Fig. 4).

Another mechanism for raising blood pressure under the action of leptin is the activation of the sympathetic nervous system under its influence, which leads not only to increased heat production and energy use [12], but also to increased blood pressure. This is confirmed by the fact of a significant correlation of leptin with the level of adrenoreactivity of the organism (r = 0.8) under conditions of increased body weight, accompanied by a change in the osmotic resistance of erythrocytes under the influence of beta-blockers [4]. Increased leptin levels were observed in the combination of hypertension and tachycardia [3], which can also be explained by the activation of the sympathetic nervous system. The level of leptin decreased with the treatment of hypertension, which, however, depended on the sex of the patient: in men the level of leptin decreased significantly, while in women the decrease in leptin was less pronounced. That is, patients with hypertension have a leptin-dependent mechanism of hypersympathicotonia, which changes under obesity and loses linear dependence, which is explained by the development of insulin resistance (IR) and increased secretion of angiotensin.

The pathogenesis of hypertension in metabolic syndrome (MS) involving leptin is proposed. It is based on IR and compensatory hyperinsulinemia, and further effects are realized through leptin, which correlates with body mass index, regulates hunger associated with activation of the sympathetic nervous system, endothelial dysfunction, vasoconstriction, increased total peripheral vascular resistance and cardiac resistance. with increasing sodium reabsorption and hypervolemia [11]. However, in the clinic there are often large fluctuations in the amount of leptin, which makes it difficult to interpret the data. Thus, in patients with hypertension under conditions of normal body weight, the level of leptin was 16.9 ± 15.3 ng / ml, under conditions of overweight - 15.1 ± 12.5 ng / ml, while under conditions of obesity - 56.4 ± 41.2 ng / ml [4], and significant fluctuations in the obtained levels attract attention. According to other data, the leptin levels of patients with

hypertension were 5.42 ± 0.21 ng / ml, 9.69 ± 0.25 ng / ml and 17.71 ± 1.33 ng / ml, respectively [5].

These debatable issues and uncertain levels of leptin in hypertension determine the feasibility of further research.

THE AIM

To study the relationship between leptin resistance, lipid and carbohydrate metabolism, blood pressure in pregnant women with obesity in the second trimester of pregnancy.

MATERIALS AND METHODS

Under observation were 65 women (main group) with obesity (I st. -27 women, II st. - 24 women, III st. - 14 women) in the II trimester of pregnancy, who were hospitalized in the Department of Pathology of Pregnancy KNP «Maternity Clinical House №1 "in Lviv during 2017-2020 on preeclampsia of varying severity, which were sent for inpatient treatment by women's clinics. The control group consisted of 30 healthy pregnant women without obesity. Patients were randomized by age and pathology.

Determination of leptin was performed by enzyme-linked immunosorbent assay (ELISA) on a TESAN spectrophotometer using the LDN Leptin ELISA test system (Germany).

The degree of obesity was determined by the body mass index (BMI) - height-weight ratio, which is determined by the formula: weight in kilograms (m) divided by height in m^2 (h).

$$BMI = \frac{m}{h^2}$$

The weight at BMI from >18.5 to <25 kg / m2 is considered normal. If the BMI is > 30-35 kg / m2– it is obesity of the 1st degree, with BMI > 35-40 kg / m2– obesity of the 2nd degree, with BMI > 40 kg / m2– of obesity of the 3rd degree. The results were calculated by the methods of parametric (under Gaussian distribution) and nonparametric statistics.

RESULTS

The study of the somatic history of pregnant women of the main group revealed: hypertension (19 women) 30%, moderate myopia of both eyes - (13 women) 20%, anemia of pregnant women - (6 women) 10%, varicose veins of the lower extremities - (12 women) 10%, chronic tonsillitis - (6 women) 10%.

Peculiarities of reproductive history and menstrual function of the main group of pregnant women were: primary infertility - (39 women) 60%, polycystic ovary syndrome - (26 women) 40%, cervical erosion - (26 women) 40%, miscarriages - (13 women) 20%, stillborn pregnancies - (13 women) 20%, late menarche (19 women) 30%, menstrual disorders - (13 women) 20%.

Among the complications of pregnancy in women of the main group prevailed: early preeclampsia - (58 women) 90%, the threat of premature birth - (52 women) 80%, SARS - (26 women) 40%, premature discharge of amniotic fluid - (26 women) 40 %, disorders of fetal-placental blood flow - (32 women) 50%, scar on the uterus - (26 women) 40%, DFD - (26 women) 40%, premature birth - (6 women) 10%, cervical suture - (12 women) 20%.

In women of the control group somatic anamnesis was complicated by diffuse goiter - (9 women) 30%, anemia in pregnant women (3 women) 10%, varicose veins in (3 women) 10%, chronic tonsillitis in (3 women) 10%.

Among the features of reproductive history and menstrual function were primary infertility in (3 women) 10%, chronic salpingo-oophoritis in (6 women) 20%, polypectomy in (2 women) 6%, miscarriages in (1 woman) 3%, adenomyosis in (2 women) 6%, menstrual disorders in (3 women) 10%.

The course of pregnancy in women of the control group was complicated by acute respiratory viral infection (ARI) in (9 women) 30%, early preeclampsia in (6 women) 20%, the threat of premature birth (in 6 women) 20%, anemia in pregnant women (3 women) 10 %, impaired fetal-placental blood flow in (3 women) 10%.

When comparing the level of leptin in the serum of pregnant women of the control group and pregnant women of the main group with obesity of the first degree, the level of leptin in the control group was 17.12 ng / ml, in pregnant women with obesity of the first degree. - 31.16 ng / ml, which is 1.82 times more than in pregnant women without obesity ($p<0.05$).

When examining pregnant women with obesity II degree leptin levels were 2.14 times higher than in pregnant women of the control group, and in pregnant women with obesity III degree - 2.6 times, respectively ($p<0.05$).

It is noteworthy to compare the absolute value of leptin levels in pregnant women with obesity of varying degrees. Thus, in obesity of the second century. the level of leptin is higher by 8.7 ng / ml (1.3 times) in comparison with pregnant women with obesity of the first degree. With obesity of the III degree in comparison with obesity of the I degree leptin level at 17.43 ng / ml (1, 28 times), and in comparison with obesity II degree – higher by 7.8 ng / ml (1, 13 times) ($p<0.05$) (Table III).

Excessive weakness in the main group of pregnant women can be explained by the presence of digestive disorders and impaired bile secretion. Slight pain or a feeling of distension in the right hypochondrium or epigastric region was noted by (46 women) 71% of pregnant women, dyspeptic symptoms – (52 women) 80%. Ultrasound in (23 women) 15% of pregnant women showed an increase in liver size, (20 women) 31% had indications of chronic cholecystitis. A similar trend was not observed in pregnant women of the control group: liver enlargement was not detected in any case, signs of chronic cholecystitis occurred in (1 woman) 3%. That is why it was considered necessary to investigate the indicators of lipid and carbohydrate metabolism in women of prospective groups (table I). The results of the study of the lipid profile, shown in table I, indicate the presence of significant interdependence (from $p<0.05$ to $p<0.01$) of high levels of cholesterol, LDL, VLDL and atherogenic index from BMI of pregnant women.

According to Pearson's correlation analysis, blood leptin was directly correlated with BMI (r = 0.66, p<0.001), body weight (r = 0.29, p<0.05), total cholesterol (cholesterol) (r = 0). , 37, p<0,009), low-density lipoproteins (LDL cholesterol) (r = 0.33, p<0.05) and vice versa with high-density particles (HDL cholesterol) (r = -0.37, p<0, 02) (Fig. V).

Given the affiliation of the main group of women to the risk group for carbohydrate metabolism disorders during gestation, an oral glucose tolerance test was performed at the time of registration of the pregnant woman. His results showed that the level of glucose in women of the main group exceeded the corresponding values in pregnant women of the control group by 12.8% (p<0.001) in the study on an empty stomach and 10.8% after glucose loading (p = 0.004).

The results of the study of carbohydrate metabolism, shown in table II, indicate a significant interdependence (from p<0.05 to p<0.001) levels of blood glucose, C-peptide and HOMA-IR index from BMI of pregnant women.

The corresponding correlation coefficients were equal to: BMI with glucose level – r = 0.351; p<0,001, BMI with C-peptide level – r = 0,450; p<0,001, BMI with HOMA index – r = 0,1504; p = 0.036. Inverse correlations of C-peptide were found with the level of P (r = -0.169; p = 0.025). This indicated the development of obese women with IR and characteristic hormonal disorders, especially hypoprogesteronemia. Clinically, this was manifested by the threat of abortion in these women, which confirmed the idea of the components of metabolic disorders in obesity. Increased glycosylated hemoglobin was associated with a burdensome family history of type 2 diabetes.

Some researchers consider leptin to be one of the means of regulating blood pressure. This confirms the presence of sOB-R in the cells of the adrenal medulla, which may indicate the regulation of leptin synthesis of vasopressors catecholamines. At the same time, high levels of catecholamines reduce leptin secretion by activating β-adrenergic receptors. Another mechanism of increasing blood pressure under the action of leptin is the activation of the SNA, which leads not only to increased heat production and energy use, but also to increased blood pressure. [10]. Thus, in women with I degree obesity, the average blood pressure was 145/80 mm Hg, while in women with III degree obesity – 163/90 mm Hg. Art. (Table III). According to the results of blood pressure monitoring in women with III degree. obesity marked an increase in SBP and DBP, which was associated with increased leptin levels. A correlation was found between the level of leptin and SBP (r = 0.50; p = 0.05) and DBP (r = 0.42; p = 0.05).

DISCUSSION

The problem of obesity is becoming increasingly important today and poses an economic, medical and social danger to human life, regardless of social or occupational distribution, place of residence, age or gender. Only 50% of the population of Ukraine has a normal weight. Instead, more than 22% are obese. According to statistics, the mortality rate of young people due to overweight is 12 times higher than for people with normal body weight.

Compared with 1960, the caloric content of food increased by 24-26%, probably due to increased consumption of refined carbohydrates, transgenic fats, sodium, potassium, fiber, non-compliance with water regime, physical activity.

Recently, the role of adipose tissue, which is considered an endocrine and paracrine organ that produces a number of hormonally active substances - adipokines (adipose derived hormones), which cause disorders of carbohydrate and lipid metabolism, regulate inflammation and immune homeostasis, has been significantly revised [1,7, 8]. The most famous of these is leptin [8].

Leptin plays an important role in the regulation of metabolism and functions of the neuroendocrine system, including the pituitary gland, hypothalamus, adrenal glands, immune system. (Fig.2).

During pregnancy, the level of leptin in the blood rises, and after childbirth and abortion – falls. During pregnancy, leptin is additionally produced in the placenta and amniotic membranes, as well as in uterine tissues, inhibiting the contraction of uterine smooth muscle [3,8].Recently, there are data on the pleiotropic effect of leptin on reproduction and pregnancy. In particular, the expression of leptin in the placenta enhances the proliferation and differentiation of trophoblast cells. With obesity and abnormal serum leptin concentrations, there are usually pathological changes in the endometrium and a low probability of implantation of a fertilized egg in the uterus, as well as the usual miscarriage [9]. There are data on the role of leptin in the development of polycystic ovaries.

Hyperleptinemia, which is associated with overweight and obesity, is considered a risk factor for chronic oligo- or anovulation, which is caused by both insulin resistance and leptin-dependent ovarian dysfunction [19] (Fig.3). Peculiarities of reproductive history and menstrual function of the main group of pregnant women were: polycystic ovary syndrome – in 40% (26 women), miscarriages – in 20% (13 women), menstrual disorders – in 20% (13 women).

There are data in the literature on the role and importance of leptin in hypertension (AH) [4, 9, 6, 10], but they are not yet final. Thus, the determination of leptin in patients with hypertension showed that with increasing its level there is not only a progressive increase in body mass index and waist circumference, but also systolic and diastolic blood pressure (BP), insulin and insulin resistance index HOMA [5]

The results of the study of the lipid profile, shown in table 1, indicate the presence of significant interdependence (from p<0.05 to p<0.01) of high levels of cholesterol, LDL, VLDL and atherogenic index from BMI of pregnant women.

The results of the study of carbohydrate metabolism, shown in table 2, indicate a significant interdependence (from p<0.05 to p<0.001) levels of blood glucose, C-peptide and HOMA-IR index from BMI of pregnant women.

Some researchers consider leptin to be one of the means of regulating blood pressure. According to the results of blood pressure monitoring in women with III degree. obesity marked an increase in SBP and DBP, which was associated with increased leptin levels.

To summarize the results of the study, a correlational relationship between the studied parameters was identified (Table I, II, III). The marked correlations are significant, at p<0,05000.

There is a correlation between:

- the level of leptin in the serum of pregnant women and the degree of obesity;
- leptin level and BMI;
- leptin level and body weight;
- leptin levels and total cholesterol;
- leptin levels and low density lipoproteins;
- leptin levels and high density lipoproteins;
- leptin levels and SBP and DBP;
- BMI and glucose level;
- BMI and C-peptide level;
- BMI with HOMA index.

Thus, adipose tissue is an endocrine and paracrine organ that produces hormonally active substances - adipokines (adipose derived hormones), which cause disorders of carbohydrate and lipid metabolism, regulate inflammation and immune homeostasis [1,7,8], the most famous of which is leptin [8].

CONCLUSIONS

1. Obese pregnant women have elevated serum leptin levels in the second trimester compared to healthy pregnant women.
2. The content of leptin in the serum of obese pregnant women correlates with the severity of the disease ($r = 0.47$; $p<0.05$).
3. Serum leptin in obese women was directly correlated with BMI ($r = 0.66$, $p<0.001$), body weight ($r = 0.29$, $p<0.05$), total cholesterol (cholesterol) ($r = 0.37$, $p<0,009$), low-density lipoproteins (LDL cholesterol) ($r = 0.33$, $p<0.05$) and vice versa with high-density particles (HDL cholesterol) ($r = - 0.37$, $p<0.02$).
4. The results of the study of carbohydrate metabolism indicate a significant interdependence: the corresponding correlation coefficients were equal to: BMI with glucose level – $r = 0.351$; $p<0,001$, BMI with C-peptide level – $r = 0,450$; $p<0,001$, BMI with HOMA index – $r = 0,1504$; $p = 0.036$. Inverse correlations of C-peptide were found with the level of P ($r = -0.169$; $p = 0.025$). This indicated the development of obese women with IR and characteristic hormonal disorders, especially hypoprogesteronemia. Clinically, this was manifested by the threat of abortion in these women, which confirmed the idea of the components of metabolic disorders in obesity.
5. Leptin is one of the means of regulating blood pressure. A correlation was found between leptin level and SBP ($r = 0.50$; $p = 0.05$) and DBP ($r = 0.42$; $p = 0.05$).

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