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Original Article

Characteristics of metabolic homeostasis and hematological indicators in young women with menstrual disorders against the background of overweight and obesity

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Abstract

Overweight and obesity are among the leading factors of menstrual dysfunction. The aim of the study was to assess the relationship between clinical and metabolic indicators, hematological parameters and features of iron metabolism in young women with obesity and menstrual disorder. Assessment of anthropometric parameters and complex clinical and metabolic examination of 120 patients with menstrual dysfunction against the background of excess body weight (50 people – group 1), class I-II obesity (40 people – group 2) and normal body mass index (30 patients) aged from 18 to 35 years old, were carried out. The results of the study of carbohydrate metabolism, the levels of C-reactive protein, ferritin, hemogram parameters and biochemical indicators were analyzed analytically. It was found that a high body mass index (BMI) at a young age (up to 29 years) and a long smoking history are significant factors in the development of menstrual dysfunction such as oligo-hypomenorrhea, secondary amenorrhea and dysphoric premenstrual disorders. An elevated BMI, even in the case of a risk weight (overweight), is associated with an increase in the concentration of C-reactive protein, serum ferritin and insulin resistance index; the concentration of serum iron was also lower in the group of obese women. Characteristics of microcytic hypochromic anemia were found in a third of patients with obesity and menstrual dysfunction. Assessment of markers of systemic inflammation as a criterion for early detection of the progressive development of obesity is a relevant and promising direction for the optimization of preventive measures.

Keywords: menstrual disorder, obesity, insulin resistance, serum ferritin, inflammatory markers, anemia.

Introduction

The feasibility of conducting this study is caused by the growing problem of obesity globally, especially when combined with socially significant diseases such as atherosclerosis, diabetes and hypertension [1–4]. It should be noted that overweight and obesity are the leading factors of menstrual dysfunction, contributing

to the increase in the frequency of a woman's reproductive health disorders [1–4]. Modern literature reports indicate a change in the age of menarche, the pathology of menstrual function formation, a greater proportion of infertility, hyperandrogenism, the likelihood of polycystic ovary syndrome development, hyperplastic processes of the endometrium, and an earlier age of menopause in this category of patients [5, 6]. This list is complemented by such conditions as miscarriages, preeclampsia, fetal growth retardation syndrome, and high frequency of operative delivery [5, 6]. However, the pathogenesis of reproductive disorders, their metabolic and hormonal basis in women suffering from overweight and obesity are controversial and not fully understood.

Despite the significant number of scientific studies focused on finding ways to solve this medical and social problem, the views of scientists on the pathogenesis of the formation of menstrual dysfunction, foremost in overweight and obese patients, are superficial and debatable. There are still no clear risk criteria for the development of metabolic disorders; the indications for the treatment of young women aimed at reducing body weight and hormonal and metabolic correction are not defined.

The aim of the study was to assess the relationship between clinical and metabolic indicators, hematological parameters and features of iron metabolism in young women with obesity and menstrual dysfunction.

Material and methods

These scientific provisions were based on the results of a scientific study of certain parameters of metabolic homeostasis in 120 patients with menstrual dysfunction against the background of overweight (50 people – group 1) and class I-II obesity (40 people – group 2) aged from 18 to 35 years. It should be noted that at the time of inclusion in the study, 23 (57.5%) of the patients of this cohort had first-degree obesity, and 17 (42.5%) had second-degree obesity. In most of them, the waist circumference exceeded 80 cm, which is a sufficiently strong criterion for the presence of visceral obesity. The control group included 30 patients with menstrual cycle disorders and a normal body mass index (BMI). The average age of the patients was 28.2±1.8 years.

Exclusion criteria were hyperprolactinemia, nonclassical adrenal hyperplasia, androgen-producing tumors, 21-hydroxylase deficiency, Cushing's syndrome, and active thyroid disease (overt, central, and subclinical hypothyroidism and hyperthyroidism). Additional exclusion criteria were extreme values of the body mass index (BMI <18 kg/m^2 and >35 kg/m^2), a disease associated with impaired carbohydrate metabolism, type 1 diabetes, use of antihypertensive agents, oral contraceptives, anti-inflammatory and hypolipidemic drugs, nonsteroidal anti-inflammatory agents, oncology, autoimmune diseases, acute and chronic diseases that can lead to tissue hypoxia, chronic renal failure, chronic liver diseases with hepatocellular failure, vegetarianism, pregnancy and lactation.

During the study, the principles of bioethics were followed: the basic provisions of the Council of Europe Convention on Human Rights and Biomedicine, GCP (1996), the Helsinki Declaration of the World Medical Association on Ethical Principles of Scientific Medical Research with Human Participation (1964–2000), and national recommendations. All the examined patients voluntarily signed the informed consent to participate in the study. The study was conducted with the approval of the biomedical ethics commission of the Ivano-Frankivsk National Medical University of the Ministry of Health of Ukraine (protocol No. 128/22 dated 09/29/2022).

All patients were evaluated for anthropometric parameters (weight, height, waist circumference (WC) and hip circumference (HC) with the determination of the WC/HC ratio and body mass index according to G. A. Bray (BMI=weight, kg/height, m^2). Classification and selection of patients according to BMI was carried out taking into account the modified World Health Organization (WHO) criteria: 22–24 (BMI <18.5 (underweight), 18.5–22.9 (normal weight), 23.0–24.9 (risk weight, or overweight), 25.0–29.9 (obesity class I) and ≥30.0 (obesity class II). The ratio of the adipose tissue distribution was determined by waist circumference/hip circumference (WC/HC). The value of WC/HC for women >0.85 indicates the abdominal type of obesity.

In order to evaluate laboratory indicators, peripheral venous blood samples were collected after a 12-hour fast in the morning on an empty stomach from 7 a.m. to 9 a.m. during the early follicular phase of the menstrual cycle (days 2±5) in the control group and in women of the studied groups. The hemogram was determined on an automatic hematology analyzer ADVIA 120 (Siemens, Germany), biochemical parameters – C-reactive protein (CRP) and insulin – on the immunochemical system ADVIA Centaur (Siemens, Germany), glycated hemoglobin – using a reference method with analyzer D-10 (Bio-Rad Laboratories, USA).

The criterion parameters of microcytosis and hypochromic anemia were: mean corpuscular volume

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(MCV) ≤80 fl, mean corpuscular hemoglobin (MCH) ≤27.5 pg, mean corpuscular hemoglobin concentration (MCHC) ≤335 g/l in the presence of serum iron level <11.5 µmol/l, total iron-binding capacity (TIBC) of blood serum >72 µmol/l, iron transferrin saturation (ITS) <15% and serum ferritin (SF) level ≤120 ng/ml in blood serum. The level of iron in the blood serum and the total iron-binding capacity of the serum were determined using the reagent kits of SpineLab LLC, Ukraine, ITS – by the following calculation method: iron content of blood serum/TIBC 100%. The content of intracellular deposited iron was assessed by the concentration of serum ferritin using the IFA-ferritin test system produced by Alcor-Bio LLC, taking into account that the level of ferritin normally varies within a wide range – from 40 to 150 µg/l. Hyperferritinemia can be interpreted as an increase in iron depots or as a marker of the reaction of proteins in the acute phase of inflammation.

Also, regarding the laboratory criteria, the study of carbohydrate metabolism was taken into account: the data of the oral glucose tolerance test (OGTT) using the glucose oxidizing method, indicators of glycated hemoglobin (HbA1c), insulin content using the radioimmunological method (Insulin IRMAKIT kits, Beckman Coulter, Czech Republic). The glucose concentration in the blood was determined using a biosensor electrochemical analysis on a SuperGL device (Germany) and Glucocapil kits (Germany). Hyperinsulinemia (HI) was considered an increase in insulin levels above 25 µIU/ml and/or above 28.5 µIU/ml 2 hours after a glucose load. To determine insulin resistance (IR), we used NOMA-IC indices (NOMA-IC index=fasting glucose (mmol/l) x fasting insulin (µIU/ml)/22.5). HOMA-IR values were characterized as normal (sensitive to insulin) if the parameter was <2.40, borderline – between 2.40 and 3.50, and high (insulin resistant) if >3.50. Serum samples were analyzed for sex hormone-binding globulin (SHBG), as well as LH/FSH ratio>2.5 cond. units were considered as an indirect marker of polycystic ovary syndrome (PCOS).

Ultrasound examination of the pelvic organs, the size of the uterus and ovaries, the size of the midline uterine echo according to the day of the menstrual cycle (MC) was performed using an ultrasound scanner with abdominal and vaginal convex sensors with a frequency of 3.5 and 7.5 MHz, respectively.

Statistical processing was performed using the Statistica software package (StatSoft, version 10, USA) and logistic regression odds ratio (OR) with 95% confidence intervals (CI) for each variable.

Results

When analyzing the structure of menstrual cycle disorders, it was found that in 20 cases (40.0%) in group 1 and 25 cases (62.5%) in group 2 ($p<0.05$), the structure of menstrual disorders is represented by oligo-hypomenorrhea; the share of secondary amenorrhea and abnormal uterine bleeding was more significant in group 2 (17.5% and 20.0%, respectively, compared to 6.0% and 6.0% in group 1) with a statistical difference regarding abnormal uterine bleeding ($p<0.05$) (Figure 1).

It is necessary to note a significant share of premenstrual and dysphoric disorders was noticed in a third of the observations in both groups. In patients of the control group, dysmenorrhea dominated (56.7%), while other clinical forms were represented in a significantly smaller proportion. In every third patient who came to the clinic with complaints of reproductive disorders, prolonged anovulation and the formation of hyperplastic processes of the endometrium were noted

Group 1, p=50	Group 2, p=40	Control group, p=30
• Oligo-hypomenorrhea – 40.0% * ˚ • Amenorrhea – 6.0% • Abnormal uterine bleeding – 6.0% ˚ • Dysmenorrhea – 16.0% * • Premenstrual syndrome – 32.0% *	• Oligo-hypomenorrhea – 62.5% • Amenorrhea – 17.5% * • Abnormal uterine bleeding – 20.0% * • Dysmenorrhea – 5.0% * • Premenstrual syndrome – 32.5% *	• Oligo-hypomenorrhea – 6.7% • Abnormal uterine bleeding – 3.3% • Dysmenorrhea – 56.7% • Premenstrual syndrome – 13.3% *

Figure 1: The structure of menstrual disorders in patients of the studied groups, p=150. Note: * – the difference is statistically reliable against the data of the control group, $p<0.05$; ˚ – the difference is statistically reliable against the data of group 2, $p<0.05$.

in every fourth – with a recurrent nature. The prevalence of irregular menstrual cycles combined with symptoms of premenstrual dysphoric disorders was significantly higher in women aged 30–35 years, where short and infrequent menstrual cycles (oligo-hypomenorrhea) and abnormal uterine bleeding also dominated (p<0.05).

It should be noted that the described pattern of the menstrual cycle was significantly higher in patients with obesity (62.5%) thanwomen with normal BMI (p<0.05), in the case of an early menarche age (55.0%) and patients that had a long history of smoking more than 10 cigarettes per day (37.5%), which demonstrates a statistically significant relationship with age, BMI, menarche age, bad habits (smoking) (Table 1).

It should be emphasized that a group of patients with a risk weight (overweight, BMI=23.0–24.9 m^2) and menstrual dysfunction is also characterized by an increase in the proportion of poor, liquid and short-term menstrual cycles and premenstrual syndrome, while patients with obesity suffer much more often from abnormal uterine bleeding and oligo-hypomenorrhea in combination with premenstrual dysphoric disorders which is 3.6 times higher than the specified parameters in group 1 and 2.4 times higher in the control group (p<0.05).

High BMI at a young age (from 18 to 29 years) (OR – 2.14; 95% C: 1.23–3.71, p<0.05) and long-term smoking experience (OR – 5.46; 95% C: 1.79–16.53, p<0.05) are significant factors of menstrual dysfunction which deteriorates with age.

The obtained data expand the understanding of the effects of overweight and obesity as factors of the systemic chronic inflammatory process in this category of patients, as the CRP and Homa-IR concentrations differ significantly in groups of overweight and obese patients (p<0.05) (Table 2).

According to the literary sources, the inflammatory component in adipose tissue plays an important role in the development of insulin resistance, along with hyperleptinemia, because obese patients suffer from hypertrophy of adipocytes, cellular infiltration, fibrosis, impaired microcirculation, changes in adipokinin secretion with increasing nonspecific markers of inflammation, such as CRP, fibrinogen and leukocyte reaction [7, 8].

Thus, the increase in BMI, even in the case of risk weight, along with the increase of WC, an increase in the concentration of CRP and insulin resistance index are noted, which can be a trigger in the development of metabolic disorders with age without appropriate correction, and also serve as an initiating mechanism of

Table 1: Features of the anamnesis and reproductive health parameters in patients of the studied groups, p=120.

Parameters	Group 1, p=50	Group 2, p=40	Control group, p=30
Age, average value, M±m	23.9±1.4 * °	32.5±2.2	29.4±2.3
Menarche age, <13 years, %	27 (54.0)*	22 (55.0) *	7 (23.3)
13–16 years old, %	11 (22.0)*	8 (20.0) *	15 (50.0)
>17 years old, %	12 (24.0)	10 (25.0)	8 (26.7)
Smoking, %	17 (34.0)*	14(35.0) *	4 (13.3)
Age of starting smoking <18 years, %	19 (38.0)*	26 (65.0) *	4 (16.7)
Smoking > 10 cigarettes a day, %	9 (18.0) °	15 (37.5) *	2 (6.7)
Infertility and miscarriage, %	18 (36.7) * °	23 (57.5) *	5 (16.7)
Hyperplastic processes of endometrium, %	6 (12.0) *°	14 (35.0) *	-
Functional ovarian cysts, %	11 (22.0) * °	17 (42.5) *	2 (6.7)
Polycystic ovarian syndrome, %	9 (18.0) * °	15 (37.5) *	-
Hyperandrogenic conditions, %	11 (22.0)* °	17 (42.5) *	1 (3.3)
BMI (kg/m^2), m±m	23,8±0.8 * °	31.5±3.2 *	20.8±0.7
Waist circumference, M±m, cm	79.8±1.12 * °	85.6±2.18 *	76.3±1.32
Waist/thigh ratio, M±m, cond. units	0.81±0.03 °	0.96±0.01 *	0.76±0.02

Note: * – the difference is statistically reliable against the data of the control group, p<0.05; ° – the difference is statistically reliable against the data of group 2, p<0.05.

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Table 2: Metabolic and hormonal parameters of homeostasis of the studied population: women with menstrual disorders against the background of overweight and obesity, p=120.

Parameters	Group 1, p=50	Group 2, p=40	Control group, p=30
Fasting glycemia, SD, mmol/l	4.3±0.6	5.9±1.8	4.2±1.3
Insulin, mIU/ml	14.82±1.3 * °	18.92±1.4 *	9.34±0.8
Hb A1c, SD, %	6.6±0.3	6.9±0.3	5.4±0.9
HOMA IR, cond. units	2.83±0.12 * °	4.78±0.46 *	1.71±0.24
SHBG, SD, nmol/l	59.8±1.6 * °	51.2±1.4 *	69.8±1.5
LH/FSH, SD	1.9±0.16 °	2.7±0.08 *	1.6±0.14
Total testosterone, SD, nmol/l,	2.12±0.18 * °	3.9±0.48 *	1.24±0.42
Free testosterone index, SD, %	0.024±0.001 * °	0.076±0.003 *	0.018±0.001
Albumin, SD, g/l	42.3±0.48 * °	32.6±0.34 *	44.8±0.26
CRP, SD, mg/l	7.9±0.6 * °	12.9±1.9 *	3.4±1.8
CRP/albumin ratio, SD	0.16±0.06 °	0.40±0.04 *	0.08±0.02

Note: * – the difference is statistically reliable against the data of the control group, p<0.05; ° – the difference is statistically reliable against the data of group 2, p<0.05.

pathological metabolic disorders, increasing thrombogenic potential and worsening of hormonal imbalance.

Serum ferritin parameters demonstrated certain features. It was found that in the group of obese women, the level of ferritin (274.6±10.4 ng/ml) was 2.4 times higher when compared with the control group (116.7±11.2 ng/ml) (p<0.05) (Table 3).

According to modern concepts, chronic low-intensity inflammation is observed in obese patients, resulting from an increase in the mass of adipose tissue and excessive production of inflammatory mediators [7, 8]. Pro-inflammatory cytokines may contribute to an increase in ferritin synthesis in reticuloendothelial cells [9, 10], as a result of which iron absorption decreases in conditions of increased iron deposition, whether within the reticuloendothelial system or inside adipocytes. Obesity affects the metabolism of iron, reducing the concentration of the ionic form and increasing the deposited one. Clinically, this would be expected to result in a combination of consumed iron deficiency and functional iron deficiency [2, 3, 10].

Our studies confirmed that the CRP/albumin ratio, as a marker of inflammation associated with metabolic and menstrual dysfunction in overweight and obese

Table 3: Hematological parameters of blood serum of the studied population: women with menstrual disorders against the background of excess body weight and obesity, p=120.

Parameters	Group 1, p=50	Group 2, p=40	Control group, p=30
Hb, g/l	114.5±6.8	99.7±3.9 *	132.5±11.2
MCV, fl	78.0±4.2 *	73.8±3.6 *	89.4±3.5
MCHC, g/l	334.0±16.7	316.3±8.9 *	344.1±10.3
MCH, pg	26.42±1.25	22.76±1.83 *	28.70±1.23
SF, µmol/l	17.62±1.8 °	11.33±1.2 *	19.8±1.6
TIBC, µmol/l	73.2±2.3	67.8±0.9 *	73.8±1.3
ITS, %	19.7±1.3 *	18.8±1.8 *	26.8±1.6
CP, mg/dL	32.2±2.9 *	29.7±2.2 *	38.9±1.6
Serum ferritin, ng/ml	142.8±6.8 * °	274.6±10.4 *	116.7±11.2
Transferrin, g/l	2.9±0.5	3.9±0.6 *	2.3±0.2

Note: * – the difference is statistically reliable against the data of the control group, p<0.05; ° – the difference is statistically reliable against the data of group 2, p<0.05.

women, is strongly associated with the diagnosis of PCOS, significantly stronger than androgen excess or insulin resistance [11]. Obesity is known to affect the inflammatory component, but in the case of PCOS, CRP/albumin levels are higher in both main study groups against the control data ($p<0.05$).

The distribution of patients according to the main hematological indicators of erythropoiesis indicated the absence of significant differences between the groups, which makes it possible to compare them.

In the case of a combination of obesity with iron deficiency anemia, the results of the analyzes showed a slight decrease in the content of markers of systemic inflammation – C-reactive protein (up to 7.8±0.9 mg/ml and 3.4±1.8 pg/ml in the control, respectively).

One-third of the patients with obesity and menstrual dysfunction had changes characteristic of microcytic (MCV – 78.0±4.2 fl and 73.8±3.6 fl, respectively in groups), hypochromic (MCHC – 334.0±16.7 g/l and 316.3±8.9 g/l, respectively), (MCH – 26.42±1.25 g/l and 22.76±1.83 g/l, respectively) anemia (Hb 114.5±6.8 g/l and 99.7±3.9 g/l, respectively).

In every fourth obese patient, the SF levels were lower compared to the data of the control group (7.2±0.9 µmol/l and 5.4±1.2 µmol/l, respectively, according to the main groups) and ITS (9.8±2.0 and 7.7±3.3%, respectively) the indicators lower than the reference values, on the other hand, the indicator of TIBC (73.8±1.3 and 74.5±2.0 µmol/l, respectively) was higher, which according to WHO criteria, is a sign of the iron deficiency. The indicated parameters were within the reference values in the group of overweight patients.

At the same time, there was no statistically significant decrease in the parameters of iron metabolism among overweight and obese women of the studied groups; however, the results of the assessment of serum iron and serum ferritin showed statistically significant differences: the level of ferritin as a protein of the acute phase of inflammation [10] in blood serum was higher (274.6±10.4 ng/ml), and the serum iron concentration was lower (11.33±1.2 µmol/l) in the group of women suffering from obesity.

The obtained data on the correlation of the main laboratory parameters of the hemogram and iron metabolism with the BMI of the examined women of the main group showed a reliable positive connection of the ferritin protein, which occurs in chronic systemic inflammation caused by obesity [9, 10].

Analysis of the literature shows that currently, there is an accumulation of data about the biological and clinical significance of metalloproteins – ferritin (FER) and transferrin (TF) [9, 10] in the inflammatory process. A potential difference in the indicators of ceruloplasmin and transferrin in obese and overweight patients has not been established. However, the data statistically differ from the indicators of the women in the control group with a normal BMI; less pronounced changes in the indicated parameters were revealed in overweight patients [9, 10, 12]. Increased SF levels in obese patients and the tendency to increase this parameter in case of excess body weight indicate the clinical significance of this marker as a marker of systemic inflammation, which can be used in the prediction of the development of metabolic disorders with age [9, 10, 12].

Discussion

Among young women and adolescents, the neuroendocrine consequences of obesity are manifested as early onset of puberty and menarche, hyperandrogenism, irregular menstruation or amenorrhea, abnormal uterine bleeding, polycystic ovary syndrome, and a higher frequency of dysmenorrhea and premenstrual disorders [4]. Data from the US National Health and Nutrition Examination Survey (NHANES) showed an increase in the prevalence of obesity among children and adolescents aged from 2 to 19 years in recent decades from 5.2 percent to 19.3 percent, nearly one in five children [4]. Similar trends to increase the prevalence of obesity are observed worldwide. According to WHO, the tendency to increase obesity shows a three-fold increase in the percentage of children and adolescents where the parameters met the criteria of overweight or obesity [1].

Metabolic disturbances, particularly insulin resistance in obese patients, lead to compensatory hyperinsulinemia, which increases the bioavailability of sex steroids by stimulating ovarian and adrenal androgen production, decreasing the hepatic synthesis of sex hormone-binding globulin (SHBG), and increasing aromatase activity in adipocytes [13, 14]. The study of 726 Australian women aged 26–36 years found that women with a higher BMI (≥25 kg/m^2), a larger waist circumference (greater than 80 cm) and a larger waist-to-hip ratio (visceral obesity) had irregular menstrual cycles more often [13].

Obese women (BMI ≥30 kg/m^2) were twice as likely to have an irregular menstrual cycle than women with normal weight. Besides, women with a larger waist circumference and waist-to-hip ratio were more likely to have long cycles (more than 35 days). The authors demonstrated that BMI, waist circumference, and

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waist-to-hip ratio were positively associated with fasting insulin and testosterone levels and the free androgen index; and negatively associated with SHBG levels, and in turn, demonstrated an association with a higher probability of long and irregular menstrual cycles, and also had common features with one of the most common endocrinopathies – PCOS [15–17].

Higher BMI is also associated with an increased risk of premenstrual disorders, including premenstrual dysphoric disorder, at a young age [18]. A prospective study that included 1,057 adult women who developed PMS during a 10-year follow-up found a strong positive correlation between BMI and the risk of PMS, with each 1 kg/m^2 increase in BMI increasing the risk of PMS by 3 percent, and significantly higher for women with BMI ≥27.5 kg/m^2 compared to women with BMI <20.0 kg/m^2 [19].

Therefore, BMI is a critical risk factor for women's reproductive health, such as ovulation, menstruation, pregnancy and childbirth, and women who started smoking before age 19 or smoke more than 10 cigarettes per day have been shown to have a significantly higher risk of menstrual disorders [5, 6, 20]. Other studies have shown that women who smoke have a higher prevalence of both irregular and shorter menstrual cycles, lower estrogen levels, and higher follicle-stimulating hormone levels [20].

Information about the biological activity of C-peptide and its antioxidant and anti-inflammatory properties, and its ability to reduce the phenomena of endothelial dysfunction, apoptosis, and microvascular lesions using mechanisms of autocrine regulation [7, 8] has appeared in literary, scientific sources in recent years. According to the authors, visceral fat is accompanied not only by hyperproduction of insulin, but also by excessive formation of C-peptide, which has a protective effect in the early stages of metabolic disorders [7, 8].

A meta-analysis of 31 studies of metabolic homeostasis parameters allowed us to conclude that the systemic level of C-reactive protein is 96% higher in women with PCOS compared to women of the control group, which proves a scientific hypothesis about the inflammatory component in the mechanisms of the pathophysiology of PCOS [11, 13, 15, 17]. Unlike CRP, albumin is an acute-phase negative reaction protein produced by the liver, providing most of the total antioxidant capacity of normal plasma, while serum albumin levels are reduced in patients with chronic inflammation [11, 13, 15, 17]. Thus, reduced albumin levels may potentially contribute to elevated free androgens in women with PCOS and exacerbate the disease phenotype. Given the ability of CRP/albumin to simultaneously capture chronic inflammation and metabolic dysfunction in women, the authors suggested that the CRP/albumin ratio may serve as a strong predictor of PCOS in this cohort of patients [11, 13, 15, 17].

Nowadays, more and more data are being accumulated on the relationship of visceral obesity with iron metabolism disorders and its deficiency. There are data on an increase of SF, an iron-containing protein in the content that reflects iron reserves in patients with metabolic syndrome [3, 7, 12, 21, 22]. It was then that the term "dysmetabolic iron overload syndrome" (DIOS) appeared, which indicates a violation of iron homeostasis as one of the concomitant diseases in obese patients and makes it possible to distinguish a special "iron deficiency phenotype", which can be characterized by both signs of deficiency and dysmetabolic iron overload syndrome, and emphasize the importance of assessing iron status in this category of women [14, 23]. Some studies have shown elevated serum ferritin levels in overweight and obese women, indicating increased iron stores in the body, even when combined with iron deficiency anemia [14, 23]. The authors note that ferritin concentration in serum or plasma temporarily increases during inflammation, complicating its interpretation as a marker of iron status [14, 23].

According to other scientific findings, the positive association of ferritin with obesity (including abdominal obesity) can be explained by its association with adipokine. On the other hand, obesity is characterized by a state of chronic, subclinical, systemic inflammation. It is known that hepcidin, which is a regulator of iron metabolism, controls its absorption in the gastrointestinal tract, storage and distribution in tissues. The production of hepcidin increases during inflammation and hypoxia and serves as a signal that inhibits iron absorption in the intestines and stimulates its sequestration by macrophages. As a result, this leads to iron accumulation by macrophages, enterocytes and hepatocytes in the form of ferritin [14]. According to Bekri S. *et al.*, recent studies have shown that hepcidin is synthesized not only in the liver, but also in adipose tissue, and the expression of hepcidin mRNA in the adipose tissue of obese patients is increased [24].

Conclusions

It was found that high BMI at a young age (up to 29 years) (OR – 2.14; 95% C: 1.23–3.71, p<0.05) and long-term smoking experience (OR – 5.46; 95% C: 1.79–16.53,

p<0.05) are significant factors in the development of menstrual dysfunction by types of oligo-hypomenorrhea, secondary amenorrhea and dysphoric premenstrual disorders.

Hematological indicators differed from the data of the control group in all parameters, a statistically significant decrease in the parameters of iron metabolism was not noted among women with obesity and overweight, but the concentration of serum iron was lower (11.33±1.2 μmol/l) in the group of women with obesity Changes characteristic of microcytic hypochromic anemia were found in a third of patients with obesity and menstrual dysfunction.

A change in BMI, even with a risk weight (overweight), is combined with an increase in the concentration of C-reactive protein, serum ferritin and insulin resistance index. The assessment of markers of systemic inflammation as a criterion for early detection of the progressive development of obesity is a relevant and promising direction for the optimization of preventive measures.

Conflict of interest

The authors declare no conflict of interest.

Consent to participate

Written informed consent was obtained from the patients.

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