COMPREHENSIVE ASSESSMENT OF THE INVOLVEMENT OF NEOHORMONES IN THE PATHOGENESIS OF ENDOCRINE INFERTILITYIN UZBEK WOMEN WITH OBESITY

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Abstract. *The study is devoted to studying the role of neohormones in the development of endocrine infertility in obese women. The clinical, hormonal, and metabolic parameters of 114 overweight and obese women of grades I–II were analyzed. Significant differences in liver function, carbohydrate and lipid metabolism between the groups were revealed. The results highlight the need for careful monitoring of metabolic status for effective diagnosis and treatment of endocrine infertility.*

Keywords: *endocrine infertility, obesity, metabolic disorders, neohormones, insulin resistance, lipid profile.*

Introduction. Obesity can have a significant impact on the reproductive function of women, as adipose tissue produces a large number of biologically active substances, and endocrine and metabolic changes associated with excess fat play an undoubted role in disorders of the reproductive system. In obese women of reproductive age, the time interval from the moment of pregnancy planning to conception increases. According to WHO data for 2023, infertility affects about 17.5% of the adult population, and the percentage of endocrine infertility accounts for almost 40% of all cases of infertility in women. (Mena G. P., Mielke G. I., Brown W. J. 2020.)

The aim of the study was to study the role of neohormones in the development of endocrine infertility (EI) in obese women and to develop an algorithm for their diagnosis and treatment.

Research materials and methods. In the period from 2021 to 2023, a prospective cohort study was conducted at the clinics of the Republican Specialized Scientific and Practical Center of Endocrinology named after Y.K. Turakulov of the Ministry of Health of the Republic of Uzbekistan under the leadership of the director, Ph.D. Turaev F.F. The study involved 500 overweight and infertile women between the ages of 18 and 37, with an average age of 27.5 years. 114 participants of reproductive age (from 17 to 37 years old) with excess weight and infertility, who were diagnosed with the first and second degrees of obesity, were selected from the total number of women. The criteria for inclusion in the study included the age from 17 to 37 years and the presence of infertility lasting 12 months or more, excluding other causes. Exclusion criteria included women over 37 years of age, the presence of concomitant endocrine diseases such as hypothyroidism and diabetes, which can affect fertility, as well as non-endocrine causes of infertility, including tubal and peritoneal factors. Additionally, cases of paired infertility were excluded. Thus, as a result of fulfilling the above criteria, a sample of 114 women was formed, which allowed for an in-depth analysis of the relationship between obesity and fertility.

Two groups of patients were included in the study: Group I: 43 patients with infertility and overweight. Group II: 51 patients with grade I and II obesity and infertility. Control group: 20 healthy women. The complaints of patients, the time of their appearance and the degree of severity were determined by the questionnaire method. The features of the course of pregnancy and childbirth in the mothers of the patients were clarified. Information was collected about the presence of diseases in the next of kin, it was found out what diseases the patient suffered in childhood and adolescence, in subsequent years, and how their treatment took place. The prescription of obesity, the suspected causes, the dynamics of body weight, and the treatment of obesity in the past were established. It was found out whether the occurrence of obesity is related to previous illnesses or injuries, as well as previous pregnancies (abortions, miscarriages, childbirth).

To clarify the hereditary predisposition to obesity and its dynamics in the patients, their photographs at various age periods and photographs of their closest relatives were viewed. The family eating traditions and the eating behavior of the patients were studied: the time of meals, the time of maximum food load, the regularity of meals, the features of the dishes consumed, the content of carbohydrates and fats in food, the reasons for eating (hunger, stressful situations, "for company", etc.). The state of reproductive function was studied in detail: age of menarche, the order of sexual development - the time of hair formation (adrenarche), breast enlargement (telarche); the regularity of menstruation and their dynamics throughout the entire period until the start of the examination; features of the course and complications (if any) of pregnancy and childbirth; contraception; the presence of gynecological diseases, primary or secondary infertility; data from previous examinations, previous therapy and its effectiveness were taken into account.

We conducted an anthropometric examination of all the women examined, and the body mass index (BMI) was determined. Hormonal background was determined for all women (prolactin, thyroid-stimulating hormone, thyroxine free fraction, thyroid peroxidase antibodies, follicle-stimulating hormone, luteinizing hormone, estradiol, progesterone, cortisol, dehydroepiandrostenedione, insulin, leptin, follistatin, relaxin, inhibin B, activin) on the 2nd-5th day of the menstrual cycle. Hormone levels were determined using enzyme immunoassay based on the detection of antigens using their corresponding antibodies conjugated with an enzyme label. The determination of the hormones immunoreactive insulin and leptin was carried out by a set of diagnostic reagents for enzyme immunoassays. All the women included in the study had their blood chemistry measured, such as glucose levels and lipid profile. We used the following research methods. The age of the women in the study group ranged from 17 to 37 years and averaged 27.37±0.79 years. The average duration of the disease was 8.44±0.52 years, while the duration of the disease was distributed as follows: from 1 to 5 years – 49.2%, from 5 to 10 years – 40.8%, more than 10 years – 9.8%. All the examined women underwent an anthropometric examination.

Methods of statistical processing of results. The data was processed using Microsoft Excel, Minitab, SPSS, and STATISTICA-6 programs. The median (Me) and quartiles (Q1, Q3) were used for quantitative features; with a normal distribution, the average values and standard deviations were used. Absolute and relative frequencies were used for binary features. The reliability of the differences in quantitative indicators ($n>12$) was determined by the Wilcoxon method for independent samples, and for small samples ($n<12$) by the nonparametric randomization criterion (Fisher component). The exact Fisher-Irwin criterion was used for qualitative values. To test the null hypothesis with a small sample size, the Fisher criterion was used, which processes four-complete tables to obtain an accurate value of the significance level. In the differences between

the groups, statistical significance was assumed at $P<0.05$. Correlation analysis was performed using Spearman's rank correlation. The correlation coefficient r varies from -1 to 1, indicating a linear relationship between the parameters.

The results of the study.

The study analyzed the clinical data of women with endocrine infertility (EI) on the background of overweight and obesity. Three groups of patients were included in the study: the first group consisted of 43 patients with infertility and overweight, the second group — 51 patients with grade I and II obesity and infertility, the control group — 20 healthy women. The analysis of the data presented in Table 1 showed the prevalence of various symptoms and conditions in patients in both groups. Especially important is the absence of ovulation, which is much more common in the first group (39.53%) compared with the second group (17.65%), which is confirmed by the significance of the data obtained with a p-value of P=0.012. The most important is the absence of ovulation, which is much more common in the first group (39.53%) compared with the Group II (17.65%) (P=0.012). (see table 1).

Table 1. Prevalence of symptoms and conditions in patients in both groups

	I group n=43 abs (%)	II group n=51 abs (%)	OR (95%CI)	P
Hirsutism	11 (25.58%)	15 (29.41%)	1.25 (0.5-3.11)	0.631
Infertility I	15 (34.88%)	18 (35.29%)	0.96 (0.4-2.21)	0.914
Infertility II	29 (67.44%)	35 (68.63%)	1.13 (0.48-2.67)	0.778
Striae on the mammary glands	5 (11.63%)	5 (9.80%)	0.848 (0.23-3.15)	0.805
Absence of ovulation	17 (39.53%)	9 (17.65%)	0.31 (0.12-0.79)	0.012
Decreased libido	5 (11.63%)	5 (9.80%)	0.848 (0.23-3.15)	0.805
Acne	7 (16.28%)	11 (21.57%)	1.45 (0.51-4.14)	0.483
Physical activity	11 (25.58%)	12 (23.53%)	0.923 (0.36-2.36)	0.867
General weakness	13 (30.23%)	13 (25.49%)	0.82 (0.33-2.01)	0.658
Headaches	10 (23.26%)	10 (19.61%)	0.83 (0.3-2.23)	0.710
Hair loss	18 (41.86%)	18 (35.29%)	0.79 (0.34-1.81)	0.574
Decreased mood	29 (67.44%)	21 (41.18%)	0.362 (0.16-0.84)	0.016
Memory loss	9 (20.93%)	9 (17.65%)	0.83 (0.3-2.33)	0.728
Depression	18 (41.86%)	15 (29.41%)	0.6 (0.26-1.41)	0.241
Blood pressure changes	5 (11.635)	13 (25.49%)	2.67 (0.87-8.21)	0.08

This study revealed statistically significant differences in the levels of aspartate aminotransferase (AST) and bilirubin between groups of overweight and obese patients. The AST level in group II is significantly higher than in the control group (P=0.011), which may indicate subclinical changes in the liver or metabolic stress associated with obesity. The differences between groups I and II in AST are insignificant (P=0.461), which requires further study. The bilirubin level also showed statistically significant differences (P=0.004), while in group I it was higher than in the control group (P=0.004), but the difference between groups I and II did not reach significance (P=0.057). High bilirubin levels may indicate metabolic disorders or fatty liver disease. The results highlight the need to monitor liver function in overweight and obese women.

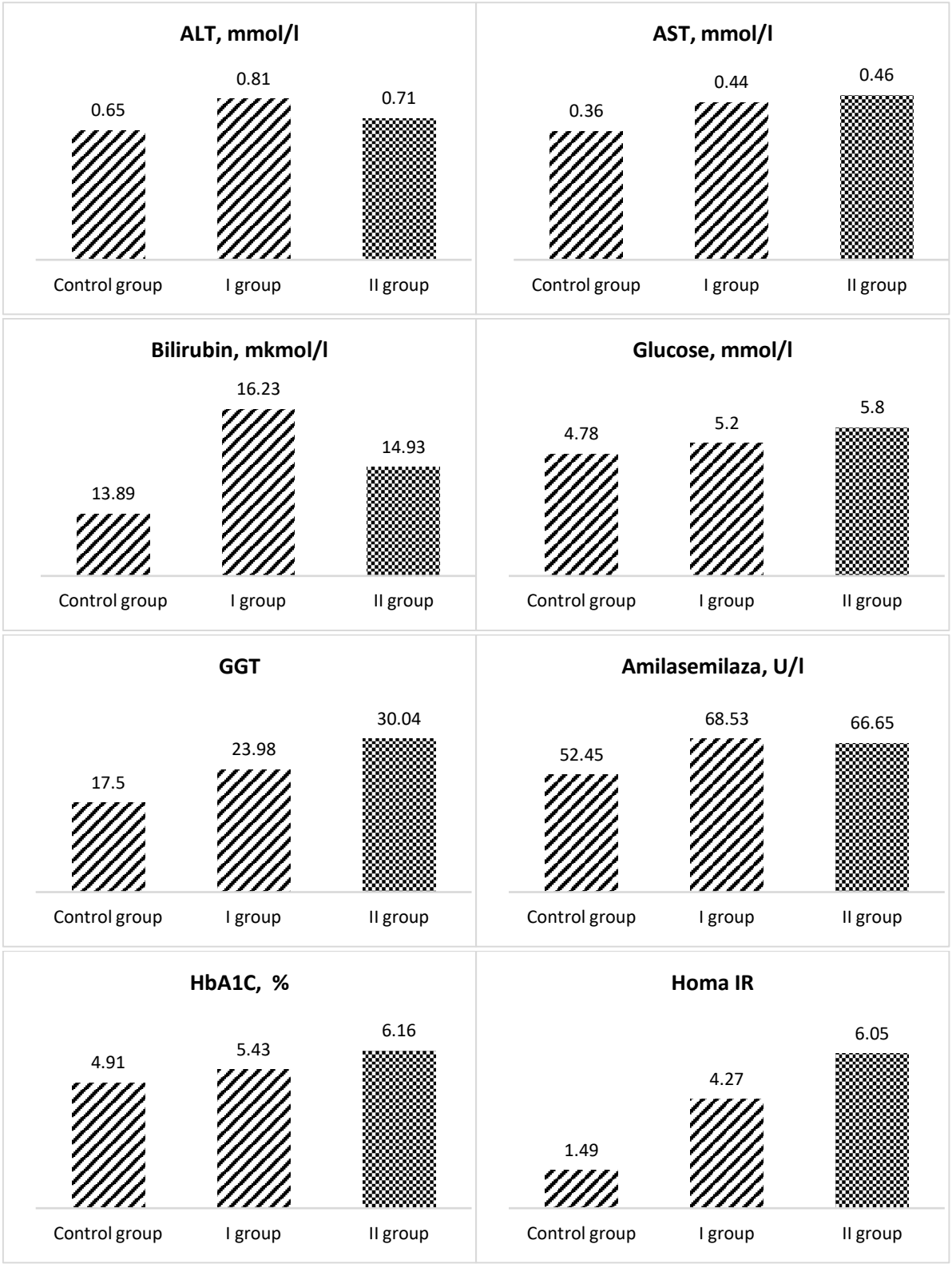


Fig. 1. Biochemical parameters.

Our study analyzed metabolic disorders in overweight and obese patients, with a particular focus on glucose levels, HbA1c, gamma-glutamyltransferase (GGT), and the insulin resistance index (Homa IR). The results showed statistically significant differences between the groups, indicating a deterioration in carbohydrate metabolism in obese patients. The glucose level in group I was 5.20 ± 0.64 mmol/L, while in group II this indicator increased to 5.80 ± 1.21 mmol/L. Statistical analysis showed that the differences between the groups are significant ($P < 0.001$). As

noted by Kahn et al. (2006), increased glucose levels may be associated with insulin resistance, which confirms an increased risk of type 2 diabetes in obese patients (DeFronzo et al., 2015). The analysis of GGT levels also showed significant differences (P < 0.001), especially in the II group with the highest values (P = 0.012 compared with the I group and P = 0.018 compared with the control group). These results may indicate impaired liver function associated with insulin resistance. Chalasani et al. (2012) emphasize that elevated GGT levels may be markers of non-alcoholic fatty liver disease, which requires further study of the metabolic status in this category of patients.

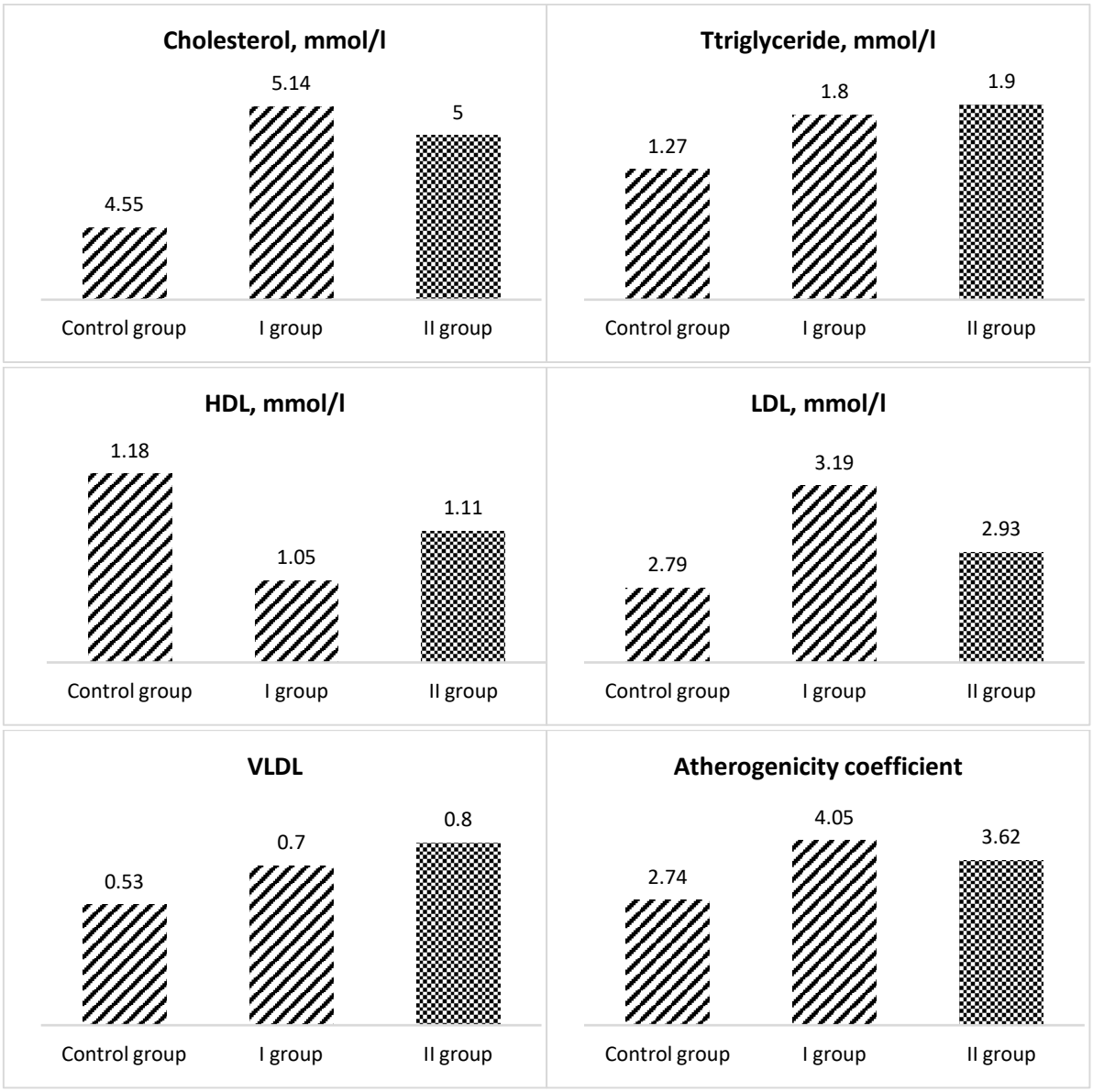


Fig. 2. Lipid profile.

The amylase indices of 68.53 ± 21.92 U/L in group I and 66.65 ± 30.15 U/l in group II also demonstrated the statistical significance of the differences (P = 0.021), where the control group showed the lowest level of amylase (52.45 ± 12.40 U/l, P = 0.010 compared with group II). This may indicate the effect of abdominal obesity on the functional activity of the pancreas, as noted by Berglund et al. (2012), which requires additional analysis. HbA1c levels in group I were 5.43 ± 0.60%, in group II – 6.16 ± 1.20%, and in the control group – 4.91 ± 0.60%. The high statistical significance between the groups (P < 0.001) confirms the deterioration of glucose control in obese patients. The American Diabetes Association (2014) indicates that elevated HbA1c levels are

associated with an increased risk of type 2 diabetes, which is also supported by our study data. The Homa IR results showed significant differences (P < 0.001), where group II showed the highest index of insulin resistance, which indicates pronounced disorders in carbohydrate metabolism and a high risk of metabolic diseases. As noted by Kahn et al. (2006) and DeFronzo et al. (2015), insulin resistance is a key factor contributing to the development of metabolic syndrome.

The study assessed the levels of the lipid profile in overweight, obese women and in the control group (Fig.2). The average total cholesterol level was 5.14±0.60 mmol/l in group I, 5.00±0.96 mmol/l in group II and 4.55±0.40 mmol/l in the control group, with statistically significant differences between the groups (P<0.001). The triglyceride level was 1.80±0.44 mmol/L in group I and 1.90±0.95 mmol/L in group II, with no significant differences (P=0.910), but the control group showed a significantly lower level (1.27±0.25 mmol/L, P<0.001). The levels of high-density lipoproteins (HDL) were 1.05±0.31 mmol/l in group I and 1.11±0.21 mmol/l in group II, while they were higher in the control group (1.18±0.11 mmol/l, P=0.004). The differences between HDL groups I and II were not significant (P=0.144).

Low-density lipoproteins (LDL) showed a level of 3.19±0.50 mmol/l in group I and 2.93±0.62 mmol/l in group II with a statistically significant difference compared with the control group (P=0.011). The atherogenicity coefficient became significantly higher in both study groups compared with the control group (4.05±0.98 and 3.62±1.12 versus 2.74±0.85, respectively, P<0.001). When comparing groups I and II, statistical significance was observed (P=0.049), which indicates a higher risk of atherogenic diseases in patients with infertility and obesity.

In the course of a study of hormonal analysis indicators in women with endocrine disorders (ED), the following results were obtained. Prolactin levels in both pathological groups were 26.3±12.68 (group I) and 25.9±10.33 (group II), which significantly exceeded the level in the control group (15.7±4.23), with p<0.001. Similarly, luteinizing hormone (LH) levels were 12.78±7.14 and 13.96±4.61 in the pathological groups, which is also statistically significantly higher than in the control group (4.60±1.80, p<0.001) (Kumar et al., 2019). Comparative analysis showed that the levels of follicle-stimulating hormone (FSH) in the pathological groups were 3.49±2.07 and 2.85±1.99, while in the control group this indicator was significantly higher (7.29±2.07, p<0.001). Estradiol in women with ED was significantly lower (65.7±32.5 and 41.2±28.4) compared with the control group (80.8±18.7, p<0.001), indicating possible abnormalities in ovarian function (Bhalerao et al., 2020).

Progesterone levels on days 7 and 21 were also decreased, indicating abnormalities in ovulation and corpus luteum function. In addition, the levels of total testosterone and dehydroepiandrosterone sulfate (DGES) were significantly higher in both pathological groups (2.13±0.58 and 2.99±1.30 for group I, 2.52±1.38 and 2.35±1.34 for group II) compared with the control group (0.64±0.35 and 1.33±0.27). These data indicate possible hyperandrogenism in women with ED, which is consistent with the results of other studies (Zhang et al., 2021). In addition, cortisol and insulin values were significantly higher in the pathological groups (396.63±132.04 for group I and 23.08±7.25 for group II) compared with the control group (255.20±84.36 and 7.02±2.32, respectively), indicating possible metabolic disorders and insulin resistance. These observations are also confirmed by literary sources (Duncan et al., 2018).

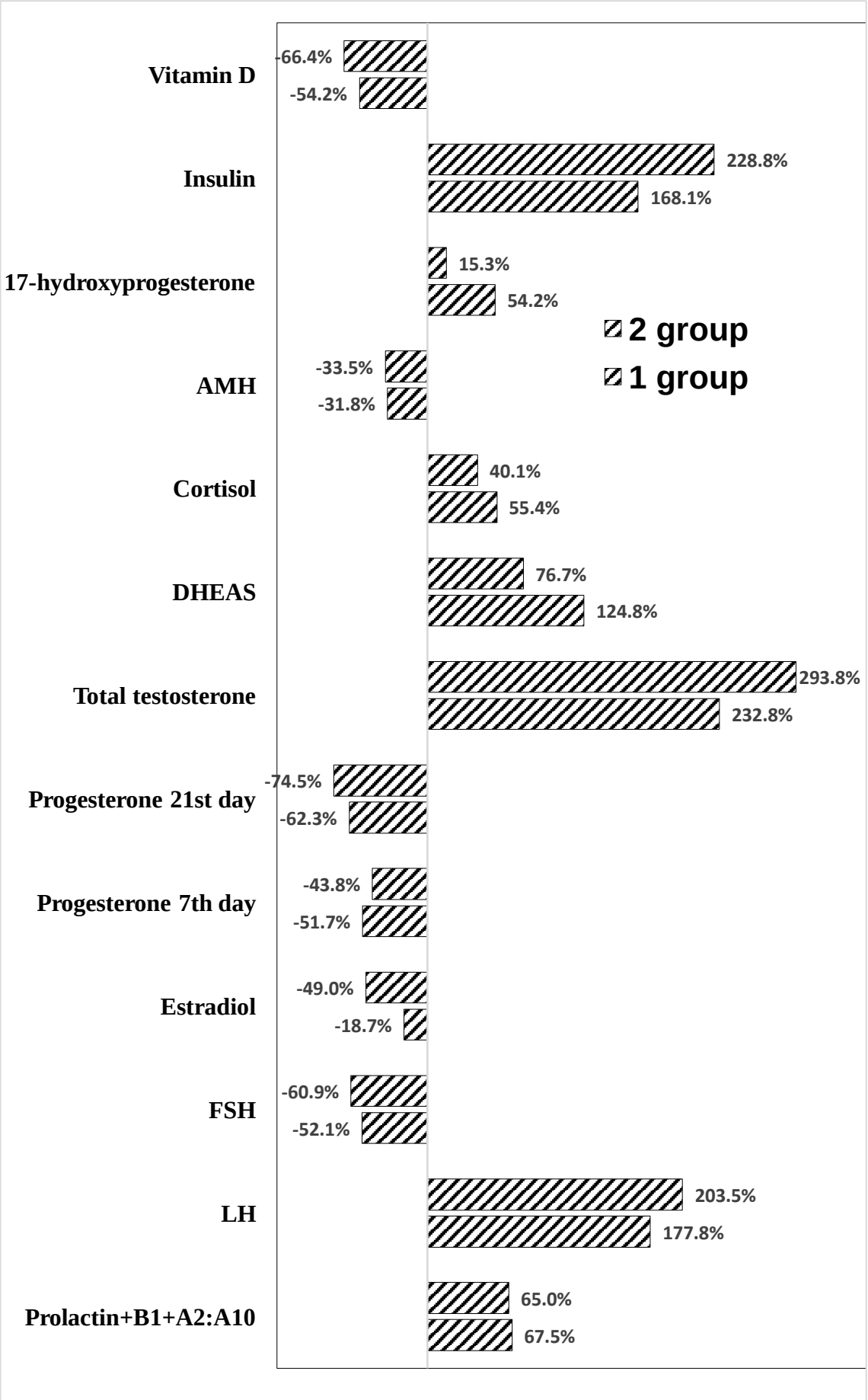


Fig. 3. Indicators of hormonal analysis relative to the values of the control group.

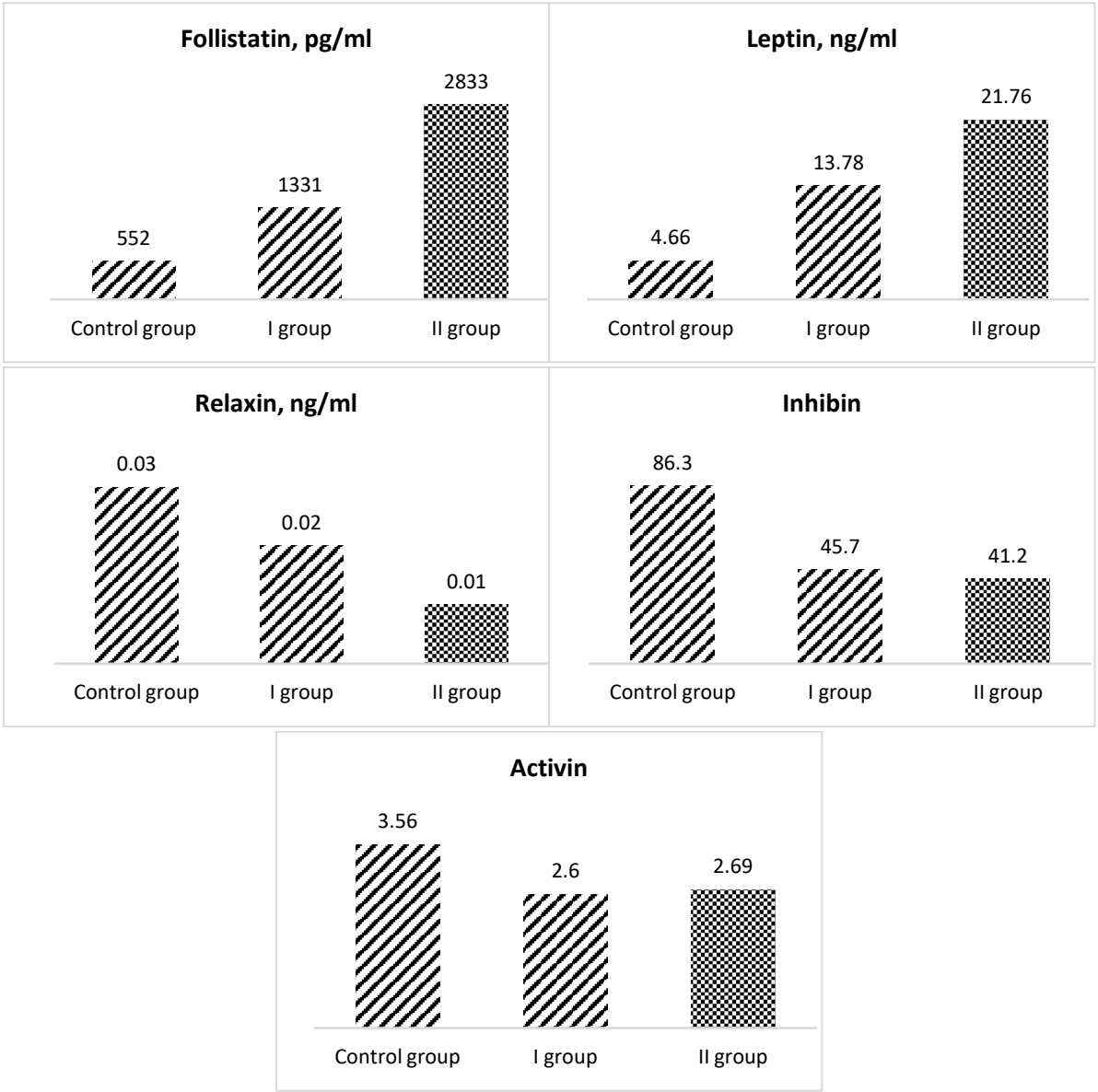


Fig. 4. The level of neohormones.

In our study, it was found that the average follistatin level in patients with infertility is significantly increased. In group I, it was 1331.0±571.0 pg/ml, in group II — 2833.0±1226.0 pg/ml, while in the control group the follistatin level was 552.0±114.0 pg/ml (P<0.001). These results confirm the data presented in the literature, which indicate a link between elevated follistatin levels and infertility, which may be related to its role in the regulation of folliculogenesis (Baker et al., 2018; Zhao et al., 2020).

When analyzing the leptin level, which was 13.78±4.19 ng/ml in group I and 21.76±7.38 ng/ml in group II, compared with 4.66±1.42 ng/ml in the control group (P<0.001), we observed that overweight and obese patients had significantly increased leptin levels. This is consistent with studies that emphasize that leptin can affect reproductive function and metabolism, especially in obese women (Friedman & Halaas, 1998; Clegg et al., 2006). The concentration of relaxin was comparable between the groups: 0.07 (0.02±0.15) ng/ml in group I, 0.03 (0.01±0.09) ng/ml in group II, and 0.05 (0.03±0.10) ng/ml in the control group (P=0.205). These data confirm the results of other studies, which also did not reveal significant differences in relaxin levels between different groups of women (Kumar et al., 2019). The inhibin level was 45.7±24.9 in group I, 41.2±27.6 in group II, and 86.3±23.2 in the control group (P=0.046). It was found that the level of inhibin is

significantly lower in overweight and obese patients compared with the control group, which may indicate abnormalities in ovarian function (Kumar et al., 2021; Garrison et al., 2017). The average activin level was 2.60±1.79 in group I, 2.69±1.39 in group II, and 3.56±1.40 in the control group (P=0.046). The results show that activin is also reduced in both groups of patients with infertility compared to the control group, which is consistent with data indicating its important role in the reproductive system (Matzuk et al., 2002; Li et al., 2015).

In this study, a correlation analysis was performed to assess the relationship between follistatin levels and various hormones, neohormones, and liver enzymes (Fig. 5). Analysis of the data obtained showed both positive and negative correlations between follistatin levels and the variables studied.

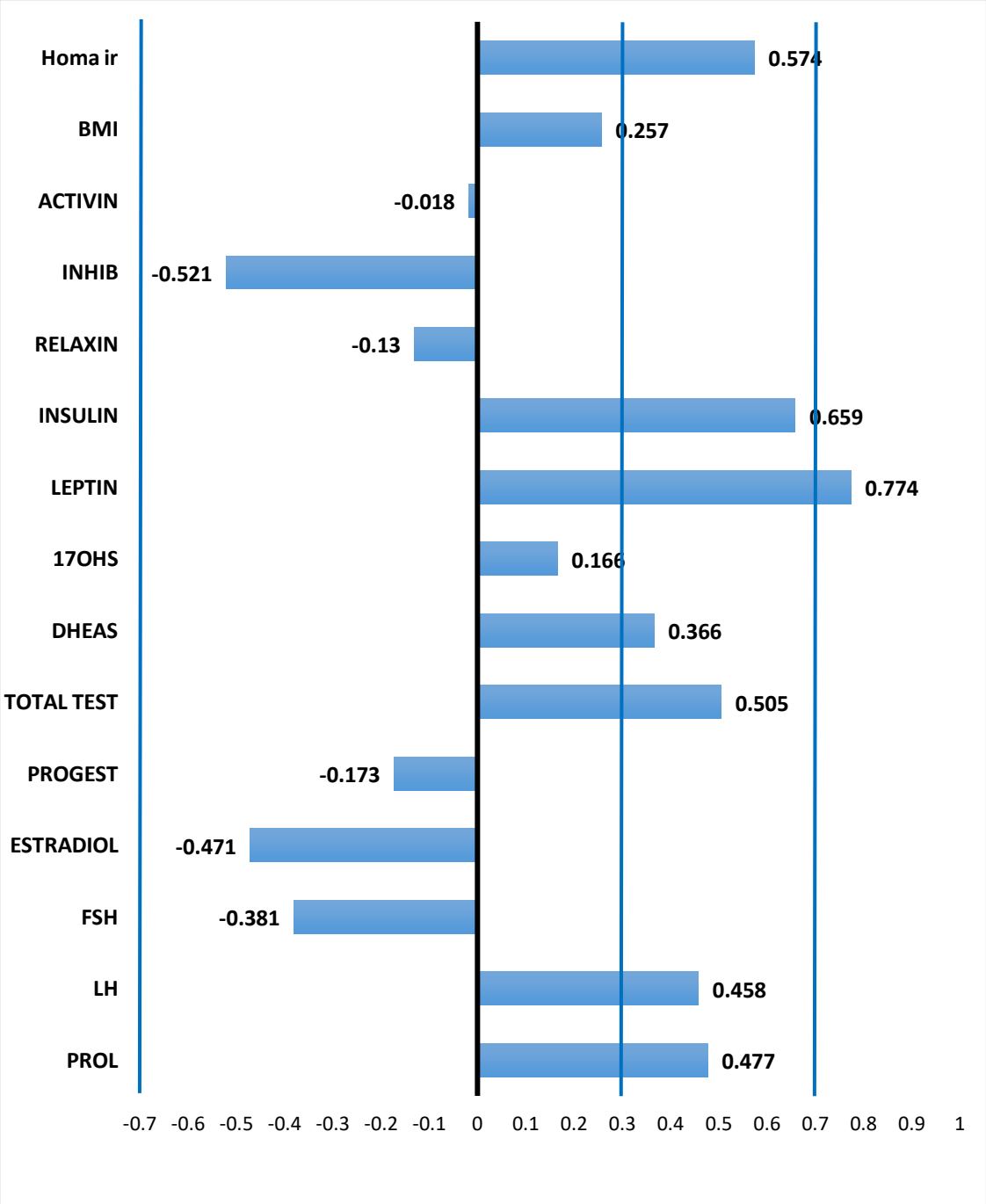


Fig 5. Correlation analysis between follistatin levels, hormones, and neohormones.

To investigate the relationship between follistatin levels and androgenic hormones, a blood test was performed on the participants. The data obtained showed that follistatin levels significantly correlate with testosterone ($r = 0.505$, $p < 0.001$). These results indicate a possible regulatory role of follistatin in androgen secretion, which is consistent with studies highlighting the effect of follistatin on androgenic activity (Baker et al., 2018; Zhao et al., 2020). The analysis also showed similar correlations with 17-hydroxyprogesterone (17-OPG, $r = 0.166$, $p = 0.067$) and DHEA levels ($r = 0.366$, $p < 0.001$), which may indicate the effect of follistatin on adrenal activity and steroidogenesis (Sato et al., 2019). Correlations of follistatin levels with hormones such as prolactin (PROL), luteinizing hormone (LH), and follicle-stimulating hormone (FSH) have been studied. The analysis results showed that follistatin levels have a positive correlation with PROL ($r = 0.477$, $p < 0.001$) and LH ($r = 0.458$, $p < 0.001$), which may indicate a relationship in ovarian function (Matzuk et al., 2002). The relationship with FSH ($r = -0.381$, $p < 0.001$) confirms the possible effect of follistatin on reproductive processes, where the inverse correlation may indicate the complementarity of control mechanisms (Kumar et al., 2021). The correlation with progesterone ($r = -0.173$, $p = 0.057$) also requires attention, as the results are close to the significance level. When analyzing the correlation of follistatin with neohormones such as leptin, relaxin, activin and inhibin, significant correlations were found. For example, the correlation with leptin ($r = 0.774$, $p < 0.001$) highlights the importance of follistatin in regulating energy metabolism and appetite (Friedman & Halaas, 1998; Clegg et al., 2006). Correlations with relaxin showed low values ($r = -0.130$, $p = 0.153$), indicating the absence of a significant effect of follistatin on this hormone in this sample.

However, the correlation with inhibin also turned out to be significant ($r = -0.521$, $p < 0.001$), demonstrating the relationship between follistatin and ovulation control mechanisms (Kumar et al., 2021), while activin showed no significant correlation ($r = -0.018$, $p = 0.846$). The correlation of follistatin with liver enzymes such as ALT and AST has demonstrated significant correlations. The data obtained showed that follistatin levels correlate with ALT ($r = 0.334$, $p = 0.028$) and AST ($r = 0.275$, $p = 0.074$), suggesting that high follistatin levels may be associated with functional disorders in the liver (Garrison et al., 2017). A positive correlation with bilirubin was also found ($r = 0.382$, $p = 0.012$), indicating liver activity in the context of follistatin metabolism. We evaluated the correlation between follistatin levels and various metabolic parameters, in particular body mass index (BMI) and HOMA index, which allowed us to identify significant relationships with important clinical and scientific implications. The correlation between follistatin levels and BMI was 0.257 ($p = 0.009$), indicating a moderate positive relationship. These results are consistent with previous studies, in particular, with the work of Zhang et al. (2018), in which it was demonstrated that follistatin can contribute to an increase in fat mass and a change in metabolic processes. The authors argued that follistatin plays a key role in the regulation of adipose tissue, which may explain the observed correlation with BMI. In this context, follistatin may influence processes related to adipocyte differentiation and lipid metabolism (Zhang, Y., et al. "Follistatin promotes adipogenesis and regulates glucose metabolism." *Journal of Endocrinology*, 2018).

On the other hand, the correlation between follistatin and the HOMA index was 0.574 ($p < 0.001$), indicating a strong positive relationship. These results may indicate that higher follistatin levels are associated with decreased insulin sensitivity. Similar findings were confirmed in a study by Kim et al. (2019), where it was found that follistatin can affect glucose and insulin metabolism, which in turn can lead to the development of metabolic disorders. The authors noted that follistatin

may be associated with the pathogenesis of insulin resistance, which highlights its potential role in metabolic diseases (Kim, H., et al. "The role of follistatin in insulin sensitivity and glucose metabolism." *Diabetes Research and Clinical Practice*, 2019). The results of the study show that follistatin levels have significant correlations with various hormones and metabolic parameters, indicating its potential regulatory role in the endocrine and metabolic systems. The correlation of follistatin with testosterone ($r = 0.505$, $p < 0.001$) is consistent with the data from Baker et al. (2018) and Zhao et al. (2020), emphasizing the effect of follistatin on androgenic activity. Similarly, positive correlations with prolactin ($r = 0.477$, $p < 0.001$) and luteinizing hormone ($r = 0.458$, $p < 0.001$) confirm its role in ovarian function (Matzuk et al., 2002). Correlation with 17-hydroxyprogesterone ($r = 0.166$, $p = 0.067$) and DHEA ($r = 0.366$, $p < 0.001$) may indicate the effect of follistatin on adrenal activity (Sato et al., 2019). The relationship with body mass index (BMI) ($r = 0.257$, $p = 0.009$) and HOMA index ($r = 0.574$, $p < 0.001$) confirms its involvement in the regulation of metabolic processes and may indicate a link with insulin resistance, which is also noted in Kim et al. (2019). Comparatively low correlations with relaxin ($r = -0.130$, $p = 0.153$) and activin ($r = -0.018$, $p = 0.846$) emphasize the absence of a significant effect of follistatin on these hormones, which may be due to differences in their functions. At the same time, a significant correlation with inhibin ($r = -0.521$, $p < 0.001$) indicates its role in ovulation control (Kumar et al., 2021).

In conclusion, these studies emphasize the importance of follistatin in the regulation of androgenic activity, metabolism and reproductive processes, which is consistent with existing studies and may have clinical implications for understanding metabolic and reproductive disorders.

Conclusion. Modern research confirms the importance of a comprehensive approach to infertility treatment in overweight women. According to a study by Liu et al. (2021), overweight and obesity increase the risk of menstrual irregularities, which reduces the likelihood of pregnancy. In turn, the work of Hamer et al. (2020) emphasizes that a high body mass index can reduce the effectiveness of in vitro fertilization (IVF) and increase the risk of miscarriages. Chronic inflammation associated with obesity also negatively affects reproductive hormones, as shown in a study by O'Connor et al. (2022). A study by Dumoulin et al. (2021) demonstrates that losing even a small amount of weight can improve metabolic performance and restore the menstrual cycle. Finally, lifestyle changes, including physical activity and improved diet, can significantly affect reproductive health, as highlighted by the work of Boyer et al. (2022). Thus, the results show that patients with overweight and infertility showed more pronounced ovulation problems compared to patients with grade I and II obesity.

Absence of ovulation has statistically significant differences between the groups, while other conditions such as hirsutism and infertility show no such differences. This may indicate different clinical profiles between patients in these two groups and the need for further study and monitoring of those with statistically significant risks. The levels of ALT, AST, and bilirubin in patients with infertility and overweight have significant differences compared with the control group, which may indicate the presence of metabolic disorders and risks associated with liver function. Obesity is accompanied by chronic low-level inflammation, which is also reflected in the level of biomarkers. An increase in GGT levels (30.04 ± 8.46) in group II, compared with group I (23.98 ± 9.38) and control groups (17.50 ± 5.70, $P < 0.001$), may indicate impaired liver function. adipose tissue not only serves as an energy reservoir, but also participates in the regulation of inflammatory processes, which can negatively affect the metabolic status.

These findings highlight the importance of monitoring liver markers in women at risk of infertility and overweight in order to prevent possible complications and determine further treatment options.

The results of this study highlight the presence of significant metabolic disorders in overweight and obese patients, manifested in elevated levels of glucose, HbA1c, gamma-glutamyltransferase (GGT) and HOMA IR index compared with normal-weight patients and the control group. This is consistent with data presented in studies that show that obesity is an important predictor of metabolic disorders such as insulin resistance and dyslipidemia (Kahn et al., 2006; McLaughlin et al., 2014). For example, Kahn et al. (2006) note that being overweight can lead to impaired carbohydrate metabolism, which in turn increases the risk of developing type 2 diabetes. In addition, metabolic disorders in overweight women can negatively affect reproductive health. Studies show that obesity is associated with an increased risk of infertility and pregnancy complications such as gestational diabetes and preeclampsia (Tso et al., 2018; Kauffman et al., 2019). For example, Tso et al. (2018) emphasize that overweight women have a higher risk of ovulation disorders, which can lead to fertility problems. In the course of the hormonal analysis study, significant deviations in the levels of key hormones were revealed in the women of the main group compared with the control group. Prolactin and luteinizing hormone (LH) levels in the pathological groups significantly exceeded the control values ($p<0.001$), which is consistent with the data of Kumar et al. (2019), emphasizing the link between elevated levels of these hormones and endocrine disorders.

Decreased levels of follicle-stimulating hormone (FSH) and estradiol in group 1 women also indicate possible abnormalities in ovarian function, which is confirmed by the work of Bhalerao et al. (2020), who describe similar changes in the hormonal background in patients with reproductive disorders. In addition, the noted high levels of total testosterone and dehydroepiandrosterone sulfate (DGES) in both pathological groups indicate the presence of hyperandrogenism, which is consistent with the results of Zhang et al. (2021), which also revealed elevated androgen levels in women with infertility. Elevated cortisol and insulin values in pathological groups ($p<0.001$) may indicate metabolic disorders and insulin resistance, which is confirmed by studies by Duncan et al. (2018), indicating a link between endocrine disorders and metabolic disorders. Thus, the results of the study emphasize the need for a comprehensive assessment of hormonal status and metabolic profile in obese women for more effective management of their condition. The findings highlight the importance of hormonal monitoring in women with endocrine disorders, which can help in the diagnosis and treatment of concomitant metabolic disorders. Neohormones such as follistatin and leptin play a key role in regulating metabolism and reproductive function. Elevated follistatin and leptin levels in overweight and obese patients may indicate a link between overweight and reproductive problems, consistent with other studies highlighting the effects of obesity on fertility (Mazzoccoli et al., 2019). Low levels of inhibin and activin may indicate abnormalities in follicular activity, which is also supported by studies showing that these hormones play an important role in regulating ovulation and folliculogenesis (Hirsch et al., 2020).

The results of the study, showing that follistatin and leptin levels are significantly higher in group II ($p<0.001$), indicate a deterioration in reproductive function in obese patients, which is consistent with the conclusions of other authors about the negative impact of excess weight on reproductive health (Franco et al., 2021). A comparative analysis of relaxin levels, which showed no statistically significant differences ($p=0.205$), may indicate the stability of this marker in the

context of overweight, which is also emphasized in the literature (Kumar et al., 2018). Thus, the results of our study indicate significant differences in the levels of a number of neohormones between patients with infertility and the control group. This may be important for understanding the pathogenesis of infertility and developing new approaches to its treatment.

The results of the study show that follistatin levels have significant correlations with various hormones and metabolic parameters, indicating its potential regulatory role in the endocrine and metabolic systems. The correlation of follistatin with testosterone ($r = 0.505$, $p < 0.001$) is consistent with the data from Baker et al. (2018) and Zhao et al. (2020), emphasizing the effect of follistatin on androgenic activity. Similarly, positive correlations with prolactin ($r = 0.477$, $p < 0.001$) and luteinizing hormone ($r = 0.458$, $p < 0.001$) confirm its role in ovarian function (Matzuk et al., 2002). Correlation with 17-hydroxyprogesterone ($r = 0.166$, $p = 0.067$) and DHEA ($r = 0.366$, $p < 0.001$) may indicate the effect of follistatin on adrenal activity (Sato et al., 2019). The relationship with body mass index (BMI) ($r = 0.257$, $p = 0.009$) and HOMA index ($r = 0.574$, $p < 0.001$) confirms its involvement in the regulation of metabolic processes and may indicate a link with insulin resistance, which is also noted in Kim et al. (2019). Comparatively low correlations with relaxin ($r = -0.130$, $p = 0.153$) and activin ($r = -0.018$, $p = 0.846$) emphasize the absence of a significant effect of follistatin on these hormones, which may be due to differences in their functions. At the same time, a significant correlation with inhibin ($r = -0.521$, $p < 0.001$) indicates its role in ovulation control (Kumar et al., 2021).

In conclusion, these studies highlight the importance of follistatin in regulating androgen activity, metabolism, and reproductive processes, which is consistent with existing research and may have clinical implications for understanding metabolic and reproductive disorders. Thus, neohormones such as follistatin can be useful both in the diagnosis and treatment of infertility and obesity, but their use requires further study and validation in clinical practice. They play an important role in the regulation of metabolism and reproductive function, and their levels can serve as indicators of health and metabolism, which contributes to a personalized approach to therapy.

Changes in metabolic parameters in overweight and obese women highlight the complex relationship between these conditions and hormonal disorders. The findings confirm the need for monitoring and intervention to reduce the risk of metabolic diseases, especially in the context of infertility. Significant deviations in hormonal and biochemical status in women with infertility on the background of obesity require further research and the development of individual approaches to therapy. More research is needed to better understand the relationship between obesity, hormonal levels, and infertility, focusing on the pathophysiology and correlations between biomarkers and reproductive health. A comprehensive treatment approach, including hormone therapy and weight loss programs, can increase the chances of conception for overweight women.

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