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Hormonal Changes in Women with Menstrual-Ovarian Dysfunction Caused by COVID-19 and Innovative Approaches to its Correction

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ABSTRACT

Background. *COVID-19 has a significant impact on the reproductive system of women, including disrupting the regulation of menstrual-ovarian function.*

Aim. *To study hormonal changes in women with menstrual-ovarian dysfunction caused by COVID-19 and to develop innovative approaches for their correction.*

Materials and methods. *The study included 90 women divided into three groups according to the clinical course of COVID-19: Group I – 20 women with mild disease, Group II – 20 women with moderate severity, and Group III – 20 women with severe COVID-19. A control group of 30 healthy women was also included. Clinical, immunological, hormonal, ultrasound, and statistical methods were used in the study.*

Results. *The study showed that estradiol and progesterone levels decreased in women who had recovered from COVID-19, while levels of FSH, LH, prolactin, and testosterone increased. Among women of reproductive age who had recovered from COVID-19, hypoestrogenism was observed in 57.3%, hyperandrogenism in 17.4%, and hypoprogesteronemia in 25.3% of patients. These findings highlight the importance of an individualized approach to treatment based on identified hormonal deviations. Hormone therapy in women who had recovered from COVID-19 helped restore the ovarian-menstrual cycle in 85.3% of patients with detected hormonal abnormalities.*

Conclusion. *The study results showed that COVID-19 in women of reproductive age causes dysfunction of the hypothalamic-pituitary-ovarian system, leading to menstrual-ovarian function disorders. Corrective hormone therapy using a drug containing 0.060 mg of micronized gestodene and 0.015 mg of ethinylestradiol in women of reproductive age who recovered from COVID-19 contributed to the restoration of menstrual-ovarian function in 85.3% of patients.*

Key words: *COVID-19; ovaries; hormones; menstrual cycle disorders; Violetta®.*

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INTRODUCTION

Hormonal changes in women with menstrual-ovarian dysfunction significantly impact their overall health, quality of life, and reproductive potential [1].

These dysfunctions may arise from endocrine dysregulation or be influenced by external factors, including infections. In recent years, research interest has focused on the effects of COVID-19 on women's reproductive health, given the virus's potential to provoke both short-term and long-term changes in the endocrine system [2].

Studies indicate that COVID-19 can profoundly affect the hormonal profile and menstrual-ovarian function, leading to virus-induced endocrinopathies [3].

The virus's mechanism of action includes neuroimmune modulation and activation of inflammatory processes, disrupting the hypothalamic-pituitary-ovarian axis and causing shifts in key hormones, such as estradiol, progesterone, and anti-Müllerian hormone (AMH) [4].

These processes may account for the menstrual cycle disruptions observed in women post-COVID-19, such as dysmenorrhea, oligomenorrhea, amenorrhea, and abnormal uterine bleeding [5].

In addition to reproductive system changes, COVID-19 is associated with prolonged endocrine disorders, such as thyroid dysfunction, altered cortisol levels, and disruptions in the hypothalamic-pituitary-adrenal axis [6].

These disorders often lead to menstrual irregularities, reduced fertility, and an increased risk of complications in future pregnancies. It is essential to consider that such effects can be both acute and long-lasting, highlighting the need for a comprehensive investigation into COVID-19's impact on women's reproductive health [7].

The relevance of this study lies in the insufficient understanding of the mechanisms by which COVID-19 affects the endocrine system in women and the lack of effective approaches for correcting the identified dysfunctions. The scientific literature notes a shortage of studies on the effects of COVID-19 on sex hormone levels and long-term reproductive outcomes in women of reproductive age, underscoring the need for further research [8].

The absence of standardized recommendations for the diagnosis, treatment, and prevention of menstrual-ovarian dysfunctions in women post-COVID-19 also supports the need for innovative therapeutic approaches to restore hormonal balance and minimize potential long-term reproductive health consequences [9].

The results of this study emphasize COVID-19's significant impact on the endocrine system in women and the need for personalized correction approaches. The application of biomarkers to assess dysfunctions and monitor therapy effectiveness appears to be a promising strategy to enhance treatment success and prevention [10].

The study aims to examine hormonal changes in women with menstrual-ovarian dysfunction caused by COVID-19 and to develop innovative approaches for their correction.

MATERIALS AND METHODS

The study was conducted from 2023 to 2024 in the gynecology department of Obstetrics Complex No. 3 and the Interdistrict Perinatal Center No. 9 in Tashkent. A distinctive feature of this research was the integration of clinical data and laboratory indicators within a multidisciplinary medical center, which enabled consideration of a wide range of factors influencing women's hormonal status. Ninety women participated in the study. They were divided into three groups based on the severity of COVID-19: the first group included 20 women with mild disease, the second group — 20 women with moderate disease, and the third group — 20 women with severe COVID-19. The control group consisted of 30 healthy women without a history of COVID-19 who met the inclusion criteria.

The inclusion criteria were age between 18 and 45, confirmed COVID-19 diagnosis (positive SARS-CoV-2 PCR test), menstrual cycle disorders (dysmenorrhea, oligomenorrhea, amenorrhea, abnormal uterine bleeding), confirmed ovarian dysfunction (lack of ovulation, persistent follicles), voluntary consent to participate, and signed informed consent. A unique approach accounted for somatic diseases, allowing for the exclusion of potential data biases caused by comorbid conditions. Exclusion criteria included: age under 18 or over 45, absence of a confirmed COVID-19 diagnosis, normal menstrual cycle, no ovarian dysfunction, severe somatic diseases (e.g., cancer, significant cardiovascular diseases), pregnancy or plans to conceive within the next 6 months, refusal to participate, and hormone therapy use within the last 3 months before the study.

Standard reagent kits from Roche Diagnostics, known for their high quality and diagnostic precision, were used to measure hormone levels. The kits were specifically adapted for the MINDRAY MR-96A automated immunological analyzer, based on enzyme-linked immunosorbent assay (ELISA) technology. A unique feature of this study was the use of leptokurtosis methods to

identify deviations in hormone distribution and discriminant function analysis to assess intergroup differences. Hormonal assessments were conducted on days 3-5 and 18-21 of the menstrual cycle to measure hormone levels in different cycle phases, accounting for fluctuations. Immunological analysis was performed with calibration and quality control procedures, ensuring high data reliability.

Corrective hormone therapy was administered using a preparation containing 0.060 mg micronized gestodene and 0.015 mg ethinylestradiol. This preparation was chosen for its proven efficacy in restoring hormonal balance and normalizing the menstrual cycle in women with ovulation disorders. Dosage and treatment duration were individualized based on disease severity and patients' clinical response. Notably, correlations between hormone levels and clinical manifestations were interpreted concerning possible COVID-19 effects on the endocrine system, allowing for hypotheses regarding the pathogenesis of these disorders. Data analysis was performed using Epi Info 7.2.2.2 software and Spearman's correlation method to identify relationships between variables. For a deeper analysis of COVID-19's impact on the hormonal profile, additional methods such as covariance analysis (ANCOVA) were employed to account for potential confounding factors, and cluster analysis was used to group patients based on similar characteristics. Bayesian statistics and the STATISTICA 10.0 software package were utilized for multivariate analysis, including the evaluation of interactions among various hormonal and clinical parameters. Differences with $p<0.05$, $p<0.01$, and $p<0.001$ were considered statistically significant.

RESULTS

The mean age of the study participants was 32.5±6.3 years. Women in the early reproductive age range (18-35 years) constituted 50% of the sample, while the remaining 50% were in the late reproductive age range (36-45 years). The body mass index (BMI) among participants varied from 21.8 to 29.4 kg/m², with an average value of 25.6±3.2 kg/m². These parameters were evenly distributed across groups, eliminating the influence of age and BMI on the study results and allowing a focused examination of COVID-19's impact on menstrual-ovarian function. According to the medical history data of the participants, the following types of menstrual disorders were observed: In Group I, which included women with mild COVID-19, abnormal uterine bleeding was observed in 40% of women, oligomenorrhea in 20%, opsomenorrhea in 7%, and dysmenorrhea in 8%. In Group II, comprising 40 women with moderate COVID-19, the prevalence of abnormal uterine bleeding was 55%, oligomenorrhea was noted in 25% of patients, opsomenorrhea in 9%, and dysmenorrhea in 11%. In Group III, which included 40 women with severe COVID-19, abnormal uterine bleeding was recorded in 70% of women, oligomenorrhea in 30%, opsomenorrhea in 12%, and dysmenorrhea in 13%.

These data confirm an increasing trend in the frequency and severity of menstrual disorders with the worsening clinical course of COVID-19, suggesting the virus's significant impact on the hypothalamic-pituitary-ovarian axis in women (Fig. 1).

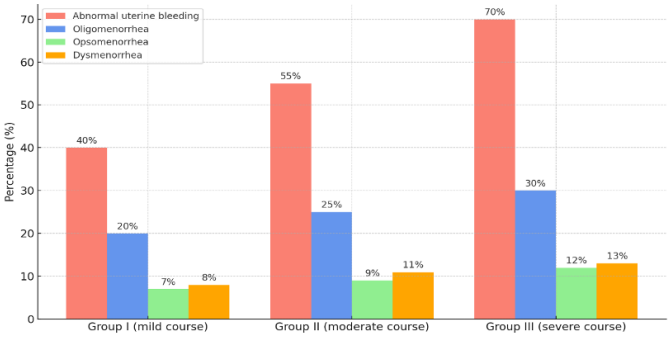

Figure 1. Frequency and types of menstrual disorders in the examined women.

Severe forms of menstrual-ovarian dysfunction, such as prolonged and heavy abnormal uterine bleeding, were more frequently observed in women who had severe COVID-19, which may indicate a potential influence of the virus on the hypothalamic-pituitary-ovarian system. These findings confirm that COVID-19 has a significant impact on women's reproductive health, especially in cases of severe illness. Further research is needed to develop methods to correct the detected disorders. The analysis of the hormonal profile in women with menstrual and ovarian dysfunction associated with COVID-19 revealed the following changes in hormone levels compared to the control group. In Group I, FSH levels were higher than in the control group, reaching 16.2±0.53 IU/ml ($P<0.001$). Elevated FSH levels were also observed in Groups II and III: 17.1±0.61 IU/ml and 18.3±0.61 IU/ml, respectively, compared to the control group (8.5±0.39 IU/ml). LH concentration was also elevated: in Group I, it was 13.5±0.43 IU/ml ($P<0.001$), in Group II — 14.2±0.46 IU/ml, and in Group III — 15.0±0.49 IU/ml, compared to the control group (8.0±0.32 IU/ml, $P<0.001$).

Estradiol concentration in Group I was lower than in the control group, at 90.0±2.9 pg/ml ($P<0.001$), in Group

II — 80.0±2.8 pg/ml, and in Group III — 70.0±2.4 pg/ml compared to the control group (210.0±10.2 pg/ml, P<0.001). Progesterone levels were also reduced: in Group I, it was 1.8±0.06 ng/ml, in Group II — 1.4±0.044 ng/ml, and in Group III — 1.2±0.04 ng/ml compared to the control group (6.2±0.22 ng/ml, P<0.001). Testosterone concentration was also elevated in the study groups compared to the control. In Group I, it was 0.94±0.03 ng/ml (P<0.05), in Group II — 1.6±0.05 ng/ml, and in Group III — 1.8±0.06 ng/ml compared to the control group (0.90±0.03 ng/ml). Prolactin levels were also elevated: in Group I, it was 25.0±0.78 ng/ml (P<0.001), in Group II — 27.0±0.85 ng/ml, and in Group III — 29.0±1.0 ng/ml (P<0.05) compared to the control group (24.0±0.9 ng/ml).

Table 1 presents the hormone levels before and after treatment with a preparation containing 0.060 mg micronized gestodene and 0.015 mg ethinylestradiol.

ml, and 8.5±0.26 IU/ml, respectively, which are comparable to the control group (8.5±0.39 IU/ml). Similar changes were observed for LH, with concentrations of 6.0±0.18 IU/ml, 6.2±0.20 IU/ml, and 6.4±0.24 IU/ml in Groups I, II, and III, respectively, compared to the control group (8.0±0.32 IU/ml). These results demonstrate a significant decrease in FSH and LH levels compared to baseline values before treatment (P<0.001).

Estradiol levels in Groups I, II, and III increased significantly after treatment, reaching 180.0±5.5 pg/ml, 170.0±5.5 pg/ml, and 160.0±5.1 pg/ml, respectively, which, although still lower than the control group level (210.0±10.2 pg/ml), indicates a positive trend in hormonal profile (P<0.001).

Progesterone levels also increased during treatment, reaching 4.5±0.14 ng/ml, 4.0±0.13 ng/ml, and 3.8±0.13 ng/ml in Groups I, II, and III, respectively, compared to the control group (6.2±0.22 ng/ml) (P<0.001). This sug-

Table 1. Hormonal profile of the examined women before and after corrective therapy with a preparation containing 0.060 mg micronized gestodene and 0.015 mg ethinylestradiol, M ± m

INDICATORS	Group I, n=20		Group II, n=20		Group III, n=20		Control Group, n=30
	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment	
FSH(mIU/ml)	16,2±0,53^^^	8,1±0,29***	17,1±0,61^^^	8,3±0,30***	18,3±0,61^^^	8,5±0,26***	8,5±0,39
LH (mIU/ml)	13,5±0,43^^^	6,0±0,18***^^^	14,2±0,46^^^	6,2±0,20***^^^	15,0±0,49^^^	6,4±0,24***^^	8,0±0,32
Estradiol (pg/ml)	90,0±2,9^^^	180,0±5,5***^	80,0±2,8^^^	170,0±5,5***^^	70,0±2,4^^^	160,0±5,1***^^^&	210,0±10,2
Progesterone (ng/ml)	1,8±0,06^^^	4,5±0,14***^^	1,4±0,044^^^	4,0±0,13***^^&	1,2±0,04^^^	3,8±0,13***^^&&	6,2±0,22
Testosterone (ng/ml)	0,94±0,030	0,85±0,027*	1,6±0,05^^^	0,87±0,03***	1,8±0,06^^^	0,90±0,03***	0,90±0,03
Prolactin (ng/ml)	25,0±0,78	22,0±0,70*^	27,0±0,85^^	23,0±0,75**	29,0±1,0^^^	24,0±0,82**&	24,0±0,90

Note: statistically significant difference compared to pre-treatment values (*-P<0.05; **-P<0.01; ***-P<0.001) ^ - statistically significant difference compared to control group (^-P<0.05; ^^-P<0.01; ^^^-P<0.001) & - statistically significant difference compared to Group I (&-P<0.05; &&-P<0.01).

After the corrective therapy with a preparation containing 0.060 mg of micronized gestodene and 0.015 mg of ethinylestradiol, significant changes were observed in the hormonal profile of the examined women. Specifically, FSH and LH levels decreased after treatment, approaching normal values, indicating stabilization of hormonal balance and restoration of the hypothalamic-pituitary-ovarian axis function. FSH concentrations in Groups I, II, and III were 8.1±0.29 IU/ml, 8.3±0.30 IU/

gests the restoration of the ovulatory cycle in patients. Testosterone and prolactin concentrations also showed positive changes.

Testosterone levels in Groups I, II, and III were 0.85±0.027 ng/ml, 0.87±0.03 ng/ml, and 0.90±0.03 ng/ml, respectively, approaching the control values (0.90±0.03 ng/ml). Prolactin levels decreased to 22.0±0.70 ng/ml, 23.0±0.75 ng/ml, and 24.0±0.82 ng/ml

in Groups I, II, and III, respectively, compared to the control group (24.0±0.9 ng/ml) (P<0.001).

These findings confirm the effectiveness of the corrective therapy with the preparation containing 0.060 mg of micronized gestodene and 0.015 mg of ethinylestradiol in normalizing hormonal balance in women with menstrual-ovarian dysfunction associated with COVID-19.

Hormonal analysis indicated that COVID-19 in women of reproductive age causes significant changes in the hypothalamic-pituitary-ovarian axis, leading to menstrual cycle disorders. Reduced levels of steroid hormones were observed: hypoestrogenism in 57.3% of patients, hypoprogesteronemia in 25.3%, and elevated testosterone levels—hyperandrogenism—in 17.4%.

These results confirm the substantial impact of COVID-19 on hormonal balance in women, with observed changes in hormone levels increasing with disease severity. The data highlight the need for an individualized approach to hormone therapy based on the specific hormonal status of each patient. To gain a deeper understanding of the relationships between COVID-19 severity and changes in the hormonal profile of patients, a correlation analysis was conducted.

The analysis results indicated significant dependencies between disease severity and levels of key hormones. In particular, a direct correlation was found between follicle-stimulating hormone (FSH) levels and COVID-19 severity (r=0.42, p<0.05), indicating that FSH levels increase with disease severity in women. This may suggest a compensatory response of the pituitary gland to decreased estradiol levels. A direct correlation was also found between luteinizing hormone (LH) levels and disease severity (r=0.44, p<0.05), confirming the disruption of the hypothalamic-pituitary-ovarian axis in response to the inflammatory response to infection.

An inverse correlation was found between estradiol levels and COVID-19 severity (r=-0.24, p<0.05), indicating a decrease in estradiol levels in patients with more severe forms of the disease. This may suggest ovarian dysfunction and suppression of hormonal activity. A similar inverse correlation was observed between progesterone levels and COVID-19 severity (r=-0.24, p<0.05), supporting data on hypoprogesteronemia in patients with severe forms of infection and indicating impaired luteinization.

A direct correlation between testosterone levels and COVID-19 severity (r=0.40, p<0.05) indicates hyperandrogenism, which is more common in patients with severe forms of the disease and may be associated with androgen metabolism disruption. A direct correlation between prolactin levels and COVID-19 severity (r=0.43, p<0.05) may be a result of the body's stress response to infection, as well as dysregulation of the pituitary gland.

These correlations highlight the significant impact of COVID-19 severity on endocrine function in women and indicate the need for further research to determine the causal mechanisms between virus-induced inflammatory processes and changes in the hormonal profile. This data also opens up new opportunities for therapeutic interventions aimed at correcting hormonal imbalances in COVID-19 patients.

Considering that patients who have recovered from COVID-19 are at an increased risk of developing thromboembolic complications, we also conducted a hemostasiogram study. The hemostasiogram analysis was performed before treatment and two weeks after taking the preparation containing 0.060 mg of micronized gestodene and 0.015 mg of ethinylestradiol.

The results of the hemostasiogram study before treatment showed that the mean APTT value in patients in the first group was 36.6±1.2 seconds, in the second group — 36.7±1.2 seconds, and in the third group — 37.7±1.3 seconds, which was significantly higher compared to the control group (27.4±0.92 seconds, p<0.001).

The D-dimer level before treatment was 243.1±8.1 ng/ml in the first group, 243.4±8.6 ng/ml in the second group, and 243.8±8.5 ng/ml in the third group, which was also higher compared to the control group (242.0±8.6 ng/ml, p<0.01). Before treatment, the fibrinogen level was 3.6±0.11 g/l in the first group, 3.7±0.12 g/l in the second group, and 3.8±0.13 g/l in the third group, whereas in the control group it was 3.5±0.13 g/l (p<0.001). The prothrombin index before treatment was 106.0±3.2% in the first group, 107.0±3.5% in the second group, and 107.4±3.6% in the third group, which was higher compared to the control group (105.0±3.6%, p<0.001).

Before treatment, the mean thrombin time was 21.5±0.73 seconds in the first group, 22.7±0.74 seconds in the second group, and 22.8±0.78 seconds in the third group, which was higher compared to the control group (21.1±0.68 seconds, p<0.01). The average platelet level before treatment was 452.0±14.6x10^9/l in the first group, 454.0±15.0x10^9/l in the second group, and 458.0±15.2x10^9/l in the third group, which was significantly higher compared to the control group (332.2±10.6x10^9/l, p<0.001). Table 2 shows changes in hemostasis parameters before and after treatment, where it is seen that taking the preparation was accompanied by a slight increase in D-dimer levels and a less pronounced increase in prothrombin and fibrinogen levels.

Table 2. Hemostasis parameters in examined women before and after corrective therapy with a preparation containing 0.060 mg micronized gestodene and 0.015 mg ethinylestradiol, M± m

INDICATORS	Group I, n=20		Group II, n=20		Group III, n=20		Control Group, n=30
	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment	
APTT (sec)	36,6±1,2^^^	36,5±1,1^^^	36,7±1,2^^^	36,4±1,1^^^	37,7±1,3^^^	36,5±1,2^^^	27,4±0,92
D-dimer (ng/ml)	243,1±8,1	243,0±8,0	243,4±8,6	243,1±8,5	243,8±8,5	243,2±8,3	242,0±8,6
Fibrinogen (g/l)	3,6±0,11	3,5±0,10	3,7±0,12	3,6±0,11	3,8±0,13	3,6±0,12	3,5±0,13
PTI (%)	106,0±3,2	105,0±3,1	107,0±3,5	105,2±3,4	107,4±3,6	106,0±3,5	105,0±3,6
Thrombin Time (sec)	21,5±0,73	21,0±0,66	22,7±0,74	21,0±0,66	22,8±0,78	21,0±0,71	21,1±0,68
Platelets (x10^9/l)	452,0±14,6^^^	447,0±14,5^^^	454,0±15,0^^^	448,0±14,5^^^	458,0±15,2^^^	450,0±14,7^^^	332,2±10,6^^^

Note: ^^^ - significant difference compared to control group (P<0.001).

Two weeks after treatment, APTT values changed as follows: in Group I — 36.5±1.1 sec, in Group II — 36.4±1.1 sec, and in Group III — 36.5±1.2 sec, which remained significantly higher compared to the control group (27.4±0.92 sec, p<0.001). The D-dimer level after two weeks was 243.0±8.0 ng/ml in Group I, 243.1±8.5 ng/ml in Group II, and 243.2±8.3 ng/ml in Group III, which was higher compared to the control group (242.0±8.6 ng/ml, p=0.01).

The fibrinogen level after two weeks was 3.5±0.10 g/l in Group I, 3.6±0.11 g/l in Group II, and 3.6±0.12 g/l in Group III, which remained higher compared to the control group (3.5±0.13 g/l, p<0.001). The prothrombin index (PTI) after two weeks was 105.0±3.1% in Group I, 105.2±3.4% in Group II, and 106.0±3.5% in Group III, which was higher compared to the control group (105.0±3.6%, p<0.001).

Thrombin time after two weeks was as follows: 21.0±0.66 sec in Group I, 21.0±0.66 sec in Group II, and 21.0±0.71 sec in Group III, which remained higher compared to the control group (21.1±0.68 sec, p=0.01). Platelet levels after two weeks were 447.0±14.5x10^9/l in Group I, 448.0±14.5x10^9/l in Group II, and 450.0±14.7x10^9/l in Group III, which were significantly higher compared to the control group (332.2±10.6x10^9/l, p<0.001).

The results indicate that treatment with a preparation containing 0.060 mg of micronized gestodene and 0.015 mg of ethinylestradiol did not significantly impact the hemostatic system, though slight changes were observed in some parameters. This confirms the safety and effectiveness of the treatment. The administration of the preparation was associated with a slight increase in D-dimer levels and a less pronounced rise in prothrombin and fibrinogen levels (p<0.001). PTI remained unchanged in both groups. Thus, the use of the preparation containing 0.060 mg of micronized gestodene and 0.015 mg of ethinylestradiol demonstrated minimal impact on hemostatic parameters. The preparation proved to have minimal influence on procoagulant activity, which is important for patients with COVID-19 at high thrombotic risk.

Ultrasound data from the women involved in the study before treatment showed the presence of immature or persistent follicles without signs of ovulation by the 22nd day of the menstrual cycle in both groups. In Group I, 74% of patients exhibited an ultrasound pattern characterized by numerous small antral follicles, the absence of a dominant follicle, and consequently, the absence of ovulation. This suggests potential disruptions in the early stages of folliculogenesis, where follicles fail to mature adequately for ovulation. In Group II, 71.4% of patients had a large dominant follicle measuring between 2.5 and 2.8 cm.

This condition suggests follicle persistence, where the dominant follicle does not undergo luteinization and does not ovulate, potentially leading to anovulation, menstrual cycle disturbances, and fertility issues. In Group III, an ultrasound pattern different from the previous two groups was observed, suggesting various types of folliculogenesis and ovulation disorders.

Patients in this group showed multiple follicles (over 12) with diameters ranging from 2 to 9 mm in each

ovary, indicative of a multifollicular ovarian pattern. The average ovarian volume was increased, exceeding 10 cm^3, which is also a diagnostic criterion for multifollicular ovaries. No dominant follicle was observed, indicating a lack of normal follicular dynamics and maturation. Figure 2 presents ultrasound data, showing that in Groups I and II, dominant follicles measuring 1.8 to 2.4 cm were observed on the 12-14th day of the menstrual cycle, a normal indicator of ovulation readiness.

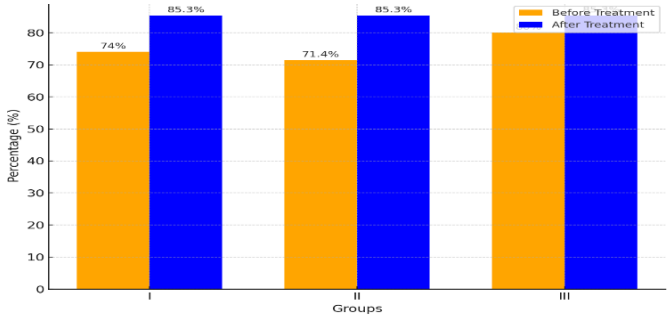

Figure 2. Dynamic of folliculogenesis in examined women before and after treatment with a preparation containing 0.060 mg micronized gestodene and 0.015 mg ethinylestradiol

The ultrasound examination results of patients after corrective hormone therapy indicated that 85.3% of women showed a restoration of normal folliculogenesis, including follicle maturation to the dominant stage and subsequent ovulation. Repeat ultrasound revealed that patients in the first and second groups had dominant follicles measuring between 1.8 and 2.4 cm on the 12th-14th day of the menstrual cycle, which is a normal indicator of ovulation readiness. Additionally, signs of ovulation, such as the presence of a corpus luteum and free fluid in the pelvic cavity, were visible on the 22nd day of the cycle in most cases. Patients in the third group, who initially had multifollicular ovaries and signs of anovulation, showed significant improvements in ultrasound parameters after corrective hormone therapy, suggesting the normalization of folliculogenesis and ovulation. 85.3% of patients experienced improvements in subjective symptoms, including menstrual cycle regularity, reduced pain, and better overall well-being.

Thus, ultrasound findings and clinical observations confirm the effectiveness of corrective hormone therapy in 85.3% of women with folliculogenesis disorders associated with persistent follicles. As a result of the treatment, 85.3% of patients achieved a restored ovulatory cycle, significantly enhancing their reproductive potential. The study also demonstrated that COVID-19 significantly affects menstrual-ovarian function in reproductive-aged women, leading to changes in key hormone levels. Corrective hormone therapy using a preparation containing 0.060 mg micronized gestodene and 0.015 mg ethinylestradiol showed high efficacy in normalizing folliculogenesis and the ovulatory cycle in 85.3% of patients. These findings highlight the need for further research and development of individualized approaches to treating hormone disorders induced by COVID-19.

DISCUSSION

The results of our study showed that COVID-19 has a significant impact on the hormonal profile and reproductive function of women of reproductive age, especially in severe cases of infection. The observed changes in levels of key hormones, such as FSH, LH, estradiol, progesterone, testosterone, and prolactin, confirm the existence of virus-induced endocrinopathies that can severely disrupt the hypothalamic-pituitary-ovarian axis. These findings align with previous studies that also indicate COVID-19's substantial impact on the endocrine system and women's reproductive health [6,7,8].

The direct correlations identified between FSH and LH levels and COVID-19 severity highlight possible compensatory mechanisms for pituitary dysfunction in response to decreased estradiol and progesterone levels. This may suggest that the infection not only disrupts ovarian function but also affects central regulatory mechanisms within the hypothalamic-pituitary-ovarian system. The inverse correlation between estradiol, progesterone levels, and disease severity confirms data on hypoestrogenism and hypoprogesteronemia in patients with severe COVID-19, which may indicate suppressed ovarian hormonal activity. A direct correlation between testosterone levels and COVID-19 severity confirms the presence of hyperandrogenism, likely resulting from disrupted androgen metabolism in response to the body's inflammatory reaction to the infection. Additionally, it is important to note that elevated prolactin levels in women with more severe forms of COVID-19 may result from stress responses and altered pituitary regulation, contributing to menstrual disturbances [2, 7].

These findings confirm that hormonal changes in women with COVID-19 are associated not only with viral load but also with disease severity. This underscores the need for an individualized approach to diagnosing and treating these patients. In particular, the observed changes in the hormonal profile and correlation analysis data could serve as a basis for developing new therapeutic strategies aimed at restoring hormonal bal-

ance and reproductive function in women who have recovered from COVID-19 [1, 4].

The application of corrective hormone therapy using a preparation containing 0.060 mg micronized gestodene and 0.015 mg ethinylestradiol demonstrated high efficacy in normalizing the hormonal background and restoring the ovulatory cycle in 85.3% of patients. These results confirm the potential for successful correction of virus-induced endocrine disorders using hormonal medications, which undoubtedly warrants further research and the development of personalized treatment protocols [7].

An interesting aspect of our study was the identification of folliculogenesis and ovulation disorders in patients with COVID-19, as confirmed by ultrasound data. The presence of persistent follicles and multifollicular ovaries in women with severe COVID-19 highlights the virus's multi-level impact on the reproductive system. It is noteworthy that the restoration of normal follicular dynamics after hormone therapy was observed in most patients, indicating a high potential for corrective treatments. However, our study has certain limitations. The relatively small sample size and the inability to conduct long-term follow-ups with patients after the completion of treatment limit the applicability of the findings to a broader population. Further studies are needed to gain a deeper understanding of the mechanisms behind these observed changes and to assess the long-term effects of COVID-19 on reproductive health. Thus, our study underscores the importance of a comprehensive approach to assessing and treating menstrual-ovarian disorders in women who have recovered from COVID-19. The findings open new avenues for developing effective therapeutic strategies aimed at restoring reproductive function and improving patients' quality of life. Future research in this area is needed to develop more accurate diagnostic and treatment methods based on the individual hormonal profile of each patient [5].

CONCLUSION

The study found that COVID-19 significantly impacts menstrual-ovarian function in reproductive-aged women, causing substantial changes in levels of key hormones. Disease severity correlates directly with increased levels of FSH, LH, testosterone, and prolactin, as well as decreased concentrations of estradiol and progesterone. The application of corrective hormone therapy using a preparation containing 0.060 mg micronized gestodene and 0.015 mg ethinylestradiol demonstrated high efficacy, facilitating the normalization of folliculogenesis and the ovulatory cycle in 85.3% of patients. These results emphasize the need for further exploration of the mechanisms by which COVID-19 affects the reproductive system and the development of individualized approaches to treating hormone disorders caused by this infection.

Ethics approval and consent to participate - All patients gave written informed consent to participate in the study.

Consent for publication - The study is valid, and recognition by the organization is not required. The author agrees to open publication

Availability of data and material - Available

Competing interests - No

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COVID-19 SABABLI MENSTRUAL-OVARIAL DISFUNKSIYASI ANIQLANGAN AYOLLARDA GORMONAL O‘ZGARISHLAR VA UNI KORREKSIYALASHDA INNOVATSION YONDASHUVLAR

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Toshkent tibbiyot akademiyasi

ABSTRACT

Dolzarbligi. COVID-19 ayollarning reproduktiv tizimiga sezilarli ta’sir ko‘rsatadi, jumladan, menstrual-ovarial funksiyani boshqarilishini buzadi.

Maqsad. COVID-19 sababli menstrual-ovarial disfunksiyaga aniqlangan ayollarda gormonal o‘zgarishlarni o‘rganish va ularni korreksiya qilishga innovatsion yondashuvlarni ishlab chiqish.

Materiallar va usullar. Tadqiqotga 90 nafar ayol jalb qilingan. Qatnashchilar COVID-19 kasalligining klinik kechishiga qarab uch guruhga bo‘lingan: I guruh – 20 nafar yengil darajadagi kasallikni o‘tkazgan ayollar, II guruh – 20 nafar o‘rtacha og‘ir kechgan ayollar va III guruh – 20 nafar og‘ir kechgan COVID-19 bilan kasallangan ayollar. Nazorat guruhiga 30 nafar sog‘lom ayollar kiritilgan. Tadqiqotda klinik, immunologik, gormonal, ultratovush va statistik usullar qo‘llangan.

Natijalar. Tadqiqot shuni ko‘rsatdiki, COVID-19 kasalligini o‘tkazgan ayollarda estradiol va progesteron darajalari pasaygan, ammo FSG, LG, prolaktin va testosteron darajalari oshgan. Reproduktiv yoshdagi COVID-19 kasalligini o‘tkazgan ayollarda gipoestrogenemiya 57,3%, giperandrogeniya 17,4% va gipoprogesteronemiya 25,3% xolatlarda qayd etilgan. Ushbu ma’lumotlar gormonal o‘zgarishlarga asoslangan individual davolash yondoshuvining ahamiyatini ta’kidlaydi. COVID-19 ni o‘tkazgan ayollarda gormonal terapiya ovarial-menstrual siklning tiklanishiga yordam berib, gormonal buzilishlar aniqlangan ayollarning 85,3% da ijobiy natija bergan.

Xulosa. Tadqiqot natijalariga ko‘ra, reproduktiv yoshdagi ayollarda COVID-19 gipotalamo-gipofizar-ovarial tizimda disfunksiyani chaqirib, menstrual-ovarial funksiya buzilishlariga sabab bo‘ladi. 0,060 mg mikronizlangan gestoden va 0,015 mg etinilestradiol saqlovchi preparat bilan gormonal korreksiyani qo‘llash COVID-19 ni o‘tkazgan reproduktiv yoshdagi ayollarda menstrual-ovarial funksiyani tiklanishiga yordam berib, 85,3% ayollarda yaxshi samara bergan.

Kalit so‘zlar: COVID-19; tuxumdonlar; gormonlar; menstrual sikl buzilishlari; Violetta®.

ГОРМОНАЛЬНЫЕ ИЗМЕНЕНИЯ У ЖЕНЩИН С МЕНСТРУАЛЬНО-ОВАРИАЛЬНОЙ ДИСФУНКЦИЕЙ, ВЫЗВАННОЙ COVID-19, И ИННОВАЦИОННЫЕ ПОДХОДЫ К ЕЁ КОРРЕКЦИИ

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АБСТРАКТ

Актуальность. Изучить гормональные изменения у женщин с менструально-овариальными дисфункциями, вызванными COVID-19, и разработать инновационные подходы к их коррекции.

Цель. Изучить гормональные изменения у женщин с менструально-овариальной дисфункцией, вызванной COVID-19, и разработка инновационных подходов к их коррекции.

Материалы и методы. В исследование были включены 90 женщин. Участницы были разделены на три группы в зависимости от клинического течения COVID-19: I группа – 20 женщин с легким течением заболевания, II группа – 20 женщин со среднетяжелым течением и III группа – 20 женщин с тяжелым течением COVID-19. Контрольную группу составили 30 здоровых женщин. Для проведения исследования использовались клинические, иммунологические, гормональные, ультразвуковые и статистические методы. Результаты. Исследование показало, что уровни эстрадиола и прогестерона у женщин, перенесших COVID-19, снизились, тогда как уровни ФСГ, ЛГ, пролактина и тестостерона увеличились. У женщин репродуктивного возраста, перенесших COVID-19, наблюдались гипоэстрогения у 57,3%, гиперандрогения у 17,4% и гипопрогестеронемия у 25,3% пациенток.

Заключение. Результаты исследования показали, что COVID-19 у женщин репродуктивного возраста вызывает дисфункцию гипоталамо-гипофизарно-овариальной системы, что приводит к нарушениям менструально-овариальной функции. Применение коррегирующей гормональной терапии препаратом, содержащим 0,060 мг микронизированный гестоден и 0,015 мг этинилэстрадиол, у женщин репродуктивного возраста, перенесших COVID-19, способствовало восстановлению менструально-овариальной функции у 85,3% пациенток.

Ключевые слова: COVID-19; яичники; гормоны; нарушения менструального цикла; Виолетта®.