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CHANGES IN THE REPRODUCTIVE SYSTEM IN WOMEN WITH THYROID GLAND PATHOLOGY AND METABOLIC SYNDROME

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Abstract
This study conducted a comparative analysis of the status of the thyroid gland and the reproductive system in women with thyroid gland pathology against the background of metabolic syndrome (MS), in contrast to a control group, based on the results of ultrasound imaging (USG) and hormonal profiling.
According to the findings, the incidence of reproductive system pathology in women with thyroid gland diseases and MS is significantly higher than in the control group. Specifically, the prevalence of uterine fibroids in the study group was 17.33% (n=26), whereas in the control group, this figure was 4% (n=2). Menstrual cycle disorders were identified in 23.33% (n=21) of patients in the study group, compared to 8% (n=4) in the control group.
An analysis of infertility cases, a key indicator of reproductive health, demonstrated that the total incidence of infertility in the study group was 6% (n=9), of which 3.33% (n=5) were diagnosed with primary infertility and 2.66% (n=4) with secondary infertility. In the control group, no cases of primary infertility were observed, while secondary infertility was recorded in 4% (n=2) of the participants.
Statistical analysis confirms that the presence of metabolic syndrome increases the risk of developing uterine fibroids by 4.3 times (an increase from 4% to

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17.33%) and underscores the significant role of metabolic disturbances in the pathogenesis of reproductive dysfunction.

Keywords: Thyroid gland, reproductive system, uterine fibroids, infertility.

Relevance of the Topic

In the 21st century, metabolic syndrome (MS) has emerged as one of the most pressing problems in global medicine and is recognized by the World Health Organization as a priority strategic direction for international healthcare [3]. Pathological conditions associated with MS, particularly endocrine and metabolic disturbances, exert a significant influence on the function of the thyroid gland (TG). From a pathogenetic perspective, it has been proven that the mitogenic effect of compensatory hyperinsulinemia—characteristic of MS—on insulin-like growth factor-1 (IGF-1) receptors in thyrocytes accelerates proliferative processes (nodular and diffuse goiter).

These processes lead to a disruption of the physiological homeostasis between the thyroid gland and the reproductive system. According to the literature, this state is a prognostic factor for the development of hormone-dependent tumors, such as menstrual cycle disorders, infertility, and uterine fibroids in women of reproductive age [9]. The complexity of the regulatory mechanisms of menstrual function under conditions of thyroid dysfunction and the direct link between menstrual cycle disorders and demographic indicators—specifically declining fertility rates—are of significant medico-social importance [12].

Full compensation of thyroid pathology is a fundamental principle in managing patients with menstrual disorders [11]. However, in regions with iodine deficiency, particularly among women with metabolic syndrome residing in the Fergana Valley, the pathogenetic interrelationship of reproductive system disorders remains insufficiently studied. Considering the above, determining the prevalence of reproductive system diseases, studying their clinical progression, and developing comprehensive diagnostic approaches for women with metabolic syndrome in the context of the severe iodine deficiency characteristic of the

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Fergana region are among the most urgent scientific and practical tasks of the present day.

Purpose of the Study

The purpose of this study is to examine changes in the reproductive system of women with metabolic syndrome based on a comprehensive assessment of thyroid functional status.

Research Object and Methods

The clinical base for the study consisted of data from 200 women aged 35 to 60 years who sought care at the Fergana branch of the Republican Specialized Scientific-Practical Medical Center (RSSPMC) of Endocrinology between 2024 and 2026, and were diagnosed with metabolic syndrome (MS). Based on the principle of representativeness, the patients were divided into two groups:

- **Group 1 (Main):** 150 women with a confirmed diagnosis of metabolic syndrome.
- **Group 2 (Control):** 50 somatically healthy women with no signs of metabolic syndrome.

In addition to standard clinical and laboratory examinations, all patients underwent a complex of diagnostic procedures aimed at assessing the functional state of the thyroid gland and the reproductive system.

Diagnostic Methods:

1. **Instrumental examination:** The anatomical and functional status of the thyroid gland, uterus, and ovaries was evaluated using high-resolution ultrasound imaging (USI).
2. **Laboratory and hormonal examination:** To determine the reproductive status of the patients, serum levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), progesterone, estrogen, and anti-Müllerian hormone (AMH) were measured using enzyme-linked immunosorbent assay (ELISA).
3. **Immunological examination:** To assess thyroid autoimmunity, the levels of antibodies against thyroid tissue were analyzed.

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All data obtained were processed using modern statistical software (Statistica or SPSS). The study was conducted in accordance with standard protocols established by the WHO and international endocrinology societies.

Results and Analysis

Palpatory analysis of thyroid gland enlargement, conducted in accordance with the World Health Organization (WHO) classification, revealed significant differences between the study groups.

In the main group (150 women with MS), 0-degree thyroid enlargement was not registered in a single case. Thyroid enlargement (thyromegaly) of the first degree was identified in 37.3% (n=56) of patients, while 62.7% (n=94) showed second-degree thyromegaly. These results indicate the presence of varying degrees of thyroid pathology in all patients within the MS group.

In the control group (50 women without MS), the indicators were relatively more favorable: 26% (n=13) had thyroid volume within the normal range (0-degree), while first- and second-degree thyromegaly were observed in 40% (n=20) and 34% (n=17) of cases, respectively.

A comparative intergroup analysis showed that against the background of metabolic syndrome, thyroid enlargement processes occur with high intensity. The fact that pathological changes were recorded in 100% of cases in the main group, and the incidence of second-degree enlargement significantly exceeded that of the control group (62.7% versus 34%), indicates the pronounced proliferative influence of metabolic disturbances on thyroid morphology (Table 1).

Table 1 Degree of thyroid enlargement in examined patients according to the WHO classification (based on palpation results)

№ Group		Thyroid enlargement grade			Total
		0-grade	I-grade	II-grade	
Group 1:	Women with metabolic syndrome (n=150)	0 (0%)	56 (37%)	94 (63%)	150 (100%)
Group 2:	Women without metabolic syndrome (n=50)	13 (26%)	20 (40%)	17 (34%)	50 (100%)
	Total	13 (6,5%)	76 (38%)	111 (55,5%)	200 (100%)

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In the next stage, morphological changes in the thyroid gland (TG) in patients were subjected to comparative analysis based on sonographic criteria from ultrasound examinations (US).

In the main group (150 women with metabolic syndrome), sonographic examination revealed a high frequency of pathological changes in TG tissues. Specifically, echographic signs characteristic of autoimmune thyroiditis were observed in 44.6% of patients (n=67). Nodular goiter was diagnosed in 5.3% of cases (n=6), mixed goiter in 7.3% (n=11), and multinodular goiter in 8% (n=12). In the control group, these indicators were statistically significantly lower: nodular goiter — 4% (n=2), mixed goiter — 4% (n=2), multinodular goiter — 4% (n=2), and autoimmune thyroiditis — 18% (n=9).

Comparative analysis of the results showed that the risk of proliferative and autoimmune processes in TG tissues is statistically higher in women diagnosed with metabolic syndrome compared to the control group. In particular, the more than 11-fold prevalence of autoimmune thyroiditis in the main group compared to the control group indicates an immunopathological influence of metabolic syndrome on thyroid tissues (Table 2).

Table 2 Thyroid pathologies identified in examined patients based on ultrasound results

Groups	Nodular goiter	Mixed goiter	Multinodular goiter	Autoimmune thyroiditis
Women with metabolic syndrome (n=150)	6 (5,3%)	11 (7,3%)	12 (8%)	67(44.6%)
Women without metabolic syndrome (n=50)	2 (4%)	2 (4%)	2 (4%)	9 (18%)
Total				

The clinical and instrumental data obtained indicate that in patients diagnosed with metabolic syndrome (MS), the frequency of proliferative processes and nodular changes in the thyroid tissue is significantly higher. Specifically, the mitogenic effect of compensatory hyperinsulinemia—characteristic of MS—on insulin-like growth factor (IGF-1) receptors in thyroid tissue manifests as one of the primary factors in the formation of multinodular goiter.

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Furthermore, the high prevalence of autoimmune thyroiditis in women in the MS group confirms the close relationship between metabolic disorders and thyroid autoimmunity. We believe the negative impact of metabolic syndrome on thyroid tissue in conditions of iodine deficiency is multifactorial. Of particular scientific significance is the fact that iodine deficiency acts as the primary "background" promoting thyrocyte hyperplasia. To deepen the understanding of the pathogenetic foundations of these processes, it is advisable to conduct additional molecular-genetic studies assessing the immunological status of thyroid hormones and the level of iodine sufficiency.

In the next stage of the study, a clinical-statistical comparative analysis of reproductive organ diseases was conducted in both groups to identify the correlation between the presence of metabolic syndrome and reproductive system pathologies (Table 3).

Table 3 Prevalence of reproductive system diseases in women of both groups

Groups	Primary infertility	Secondary infertility	Uterine fibroids	Menstrual disorders	PCOS	Total
Women with MS and TG pathology (n=150)	8 (5.3%)	6 (4%)	26 (17.33%)	21 (14%)	12 (8.0%)	73 (48,6 %)
Women without MS (n=50)	0(0%)0	2(4%)	2 (4%)	4(8%)	2 (4%)	10 (20%)
Total	8	8	28	25	14	83

Analysis of the data revealed that the frequency of reproductive system disorders in women with metabolic syndrome (MS) is statistically significantly higher than in the control group ($p<0.05–0.001$). In particular, primary infertility was diagnosed in 5.3% (n=8) of patients in the main group, while no such cases were registered in the control group ($p<0.001$). The frequency of secondary infertility was 4% (n=6) in the main group, which is comparable to the control group (4%, n=2; $p<0.05$).

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The prevalence of uterine fibroids in the main group reached 17.3% (n=26), which statistically significantly exceeds the control group (4%, n=2; p<0.001). A similar pattern was observed regarding menstrual cycle disorders (14% vs. 8%; p<0.001) and polycystic ovary syndrome (PCOS) (8% vs. 4%; p<0.001). This high frequency of pathologies in patients with MS suggests that metabolic disorders are a critical factor negatively affecting the morphofunctional state of reproductive organs.

In the next stage, the relationship between thyroid dysfunction and reproductive system pathologies was examined. The levels of thyroid-stimulating hormone (TSH), free thyroxine (T4), free triiodothyronine (T3), and anti-thyroid peroxidase antibodies (Anti-TPO) were analyzed. The goal was to determine the influence of thyroid functional state (euthyroidism, subclinical/overt hypothyroidism, or hyperthyroidism) on the risk of developing reproductive system pathologies (Table 4).

Table 4 Frequency of reproductive system diseases in women with metabolic syndrome depending on thyroid functional state

Reproductive Pathology	Euthyroidism	Subclinical Hypothyroidism	Overt Hypothyroidism	Subclinical Hyperthyroidism	Total
Primary infertility	2 (25%)	3 (37.5%)	4 (50%)	1(12.5%)	8 (100%)
Secondary infertility	1 (12.5%)	4 (50%)	3 (37.5%)	0 (0%)	8 (100%)
Uterine fibroids	15(53.57%)	8 (28.57%)	3 (10.71%)	2(7.14%)	28 (100%)
Menstrual disorders	6 (24%)	15 (60%)	1 (4%)	3(12%)	25 (100%)
PCOS	5 (35.71%)	6 (42.85%)	1 (7.1%)	2(14.2%)	14 (100%)
Total	29 (34.9%)	36 (43.37%)	12 (14.45%)	8 (9.6%)	83 (100%)

Analysis of the results confirmed that thyroid status significantly influences the development of reproductive system pathologies. Distribution based on thyroid hormone levels showed that hypothyroidism is the most significant risk factor for reproductive disorders.

Specifically, in patients with hypothyroidism (subclinical and overt), menstrual disorders were identified in 60% of cases (n=15), the highest indicator.

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Furthermore, the frequency of secondary infertility (50%; n=4), PCOS (42.85%; n=6), and uterine fibroids (28.57%; n=8) statistically significantly predominated in the hypothyroidism group.

In patients with hyperthyroidism, the frequency of these pathologies was significantly lower: infertility (12.5%; n=1), uterine fibroids (7.14%; n=2), menstrual disorders (12%; n=3), and PCOS (14.2%; n=2).

This comparative analysis demonstrates that hypothyroidism plays a leading role in the disruption of reproductive health in women with metabolic syndrome. Decreased functional activity of the thyroid gland leads to hormonal dysregulation of the "hypothalamus-pituitary-ovary" axis, acting as a catalyst for the development of myomatous processes and ovulatory dysfunction.

Conclusions

1. Morphofunctional changes in the thyroid gland were registered with a high frequency in women with metabolic syndrome (MS) compared to the control group. In particular, the detection of autoimmune thyroiditis in 44.6% of patients in the MS group confirms that metabolic disorders have a pronounced negative impact on the immunological status of the thyroid gland.
2. Metabolic syndrome is an important pathogenetic factor leading to a significant decline in reproductive health. It was established that the prevalence of uterine fibroids in patients with MS (17.3%) is 4.3 times higher than in the control group (4%). Furthermore, the high rates of primary infertility and menstrual cycle disorders ($p<0.001$) allow patients with MS to be classified as a high-risk group for the development of reproductive system pathologies.
3. The functional state of the thyroid gland is directly correlated with the clinical course of reproductive system diseases. In women with hypothyroidism, reproductive dysfunctions (menstrual cycle disorders — 60%, secondary infertility — 50%) occur significantly more frequently than in patients with hyperthyroidism. This provides a basis to consider hypothyroidism as a crucial metabolic-endocrine catalyst that exacerbates reproductive system pathologies in women against the background of metabolic syndrome.

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