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Thyroid status in patients with endometrial pathology

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Abstract. The aim of this study was to investigate the functional status of the thyroid gland in women with endometrial hyperplastic processes, in light of the increasing interest in the role of thyroid dysfunction in the aetiopathogenesis of proliferative changes in the uterine mucosa. The study included 30 women of late reproductive and perimenopausal age (14-50 years), diagnosed with various forms of endometrial hyperplastic pathology, based at the Zaporizhzhia Medical Academy of Postgraduate Education, Ministry of Health of Ukraine. The methodology involved clinical and laboratory assessment of patients, including pelvic ultrasound, histological examination of the endometrium, and evaluation of thyroid-stimulating hormone, free thyroxine and triiodothyronine levels, along with antibodies to thyroid peroxidase. The main findings demonstrated that women with endometrial hyperplasia frequently exhibited concomitant thyroid dysfunction, including subclinical or overt hypothyroidism. An elevated thyroid-stimulating hormone level (3.8 ± 1.2 mIU/L) was observed in patients with endometrial hyperplasia compared to the control group, alongside increased concentrations of thyroid peroxidase antibodies, indicating an autoimmune origin of the dysfunction. Analysis revealed a correlation between the severity of thyroid dysfunction and the morphological variant of hyperplastic endometrial changes: clinically significant thyroid dysfunction was more prevalent in women with atypical hyperplasia. These findings support the rationale for routine thyroid function screening in women with endometrial hyperplasia, to detect latent thyroid pathology, which may serve as both a background and a triggering factor in the development of proliferative endometrial disorders. Thus, the study underscores the importance of an integrated approach to the diagnosis and management of endometrial hyperplastic processes, considering the status of the thyroid gland and the endocrine system more broadly

Keywords: thyroid-stimulating hormone; menopause; thyroid dysfunction; thyroid peroxidase antibodies; tissue hyperplasia; reproductive age

INTRODUCTION

The relevance of this study lies in the high prevalence of endocrine disorders among women of reproductive age and their close association with endometrial pathology. Thyroid dysfunction can influence the menstrual cycle, fertility, and the morphofunctional state of the endometrium, thereby complicating the course of gynaecological conditions. Investigating the relationship between these disorders is essential for early diagnosis, the selection of appropriate therapy, and the prevention of complications, while also enhancing the effectiveness of comprehensive medical support for women.

Among the various disorders of the female reproductive system that are of interest to both clinical practice and scientific research, endometrial hyperplastic processes warrant particular attention. Yu.V. Strakhovetska [1] and M. Al-Kaabi *et al.* [2] examined the characteristics of

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endometrial hyperplastic processes in postmenopausal women, noting that the majority of patients (77%) presented with climacteric syndrome during the menopausal transition. In 60% of these women, certain manifestations of the syndrome persisted into the postmenopausal period. These pathologies encompass a broad spectrum of alterations in the uterine mucosa, ranging from benign proliferative changes to precancerous conditions and early-stage carcinoma. O.D. Leshchova [3] observed that gynaecological pathology most frequently occurred in women with simple endometrial hyperplasia without atypia, often accompanied by chronic endometritis, as well as in patients with chronic endometritis and reactive hyperplasia. Such cases were typically associated with urogenital infections, menstrual irregularities, and pronounced urinary tract pathology.

Despite numerous studies, the pathogenesis of endometrial hyperplastic processes remains complex and insufficiently understood. Hormonal imbalance – particularly oestrogen stimulation in the context of relative or absolute progesterone deficiency, frequently observed in anovulatory cycles – plays a significant role in the development of these changes. I.K. Orishchak *et al.* [4] emphasised the importance of infectious factors in the aetiology of endometrial hyperplastic processes. Restoration of the genital tract microbiocenosis contributes to more effective treatment and the prevention of relapses. Thyroid hormones participate in the regulation of the menstrual cycle, ovulation, endometrial development, and the maintenance of pregnancy. Thus, changes in thyroid function may directly or indirectly impact the condition of the uterine lining. I.I. Kulyk & S.V. Khmil [5] noted that correcting endocrine imbalance, particularly through the use of vitamin D3 and inositol, has a positive effect on the endometrium in hormonally dependent conditions.

There is, however, a well-established association between thyroid pathology and various gynaecological disorders, including infertility, dysfunctional uterine bleeding, polycystic ovary syndrome, and early menopause. The potential role of thyroid dysfunction in the pathogenesis of endometrial hyperplastic changes is of particular interest. Hypothyroidism – both subclinical and overt – may be accompanied by anovulation, hyperoestrogenism, and delayed secretory transformation of the endometrium, thereby creating conditions conducive to excessive proliferation of the uterine lining. G. Brenta & U. Hostalek [6] studied comorbidities associated with hypothyroidism. Autoimmune thyroiditis, one of the most common causes of hypothyroidism, may also exert additional effects via systemic inflammation and impaired immune regulation. L.J. Jara *et al.* [7] have explored the broader systemic impact of this disease in more detail. Despite the apparent pathophysiological connections, the association between thyroid status and endometrial hyperplasia remains inconsistently addressed in the literature. Some studies report a high frequency of thyroid abnormalities in patients with endometrial hyperplasia, while others do not identify significant differences relative to the general population. This discrepancy may be attributed to methodological variations across studies – such as differing designs, inclusion criteria, and classification of hyperplasia – as well as regional differences in thyroid disorder prevalence, iodine sufficiency, and socio-genetic factors.

Discussion of thyroid dysfunction in patients with endometrial hyperplasia gains particular importance in the context of gynaecological and oncological disease prevention. Given the potential for proliferative endometrial changes to undergo malignant transformation, timely correction of concomitant endocrine disorders, especially thyroid dysfunction, may serve as a valuable secondary preventive strategy against oncological complications. This is especially pertinent in high-risk populations, including women in perimenopause, those with excess body weight, metabolic syndrome, or a family history of related diseases. D.Yu. Beraya [8] observed that women with infertility and various thyroid pathologies frequently present with ovarian-menstrual disorders such as dysmenorrhoea and oligomenorrhoea. In cases of infertility, the predominant contributing factor is endometriosis in patients without thyroid pathology, whereas in those with thyroid dysfunction, the endocrine factor is more relevant.

Endometrial hyperplastic processes are common among women of late reproductive and perimenopausal age and are associated with a high risk of recurrence and malignancy. J. Huang *et al.* [9] have described oncological variants of endometrial pathology and the associated risk factors. Nevertheless, the role of thyroid dysfunction in these processes remains insufficiently understood, and current clinical protocols do not mandate thyroid function assessment. This represents a significant scientific and practical gap, which hampers the timely identification of concomitant endocrine abnormalities and reduces the effectiveness of therapeutic interventions. Aim of the study: to assess the functional state of the thyroid gland in women with endometrial hyperplastic processes and to establish a potential pathogenetic link. Objectives of the study: to determine the prevalence of thyroid pathology among patients with endometrial hyperplastic processes; to analyse the levels of thyroid-stimulating hormone (TSH), free triiodothyronine (T3), free thyroxine (T4), and antibodies to thyroid peroxidase; to identify correlations between the forms of endometrial hyperplasia and thyroid function status.

MATERIALS AND METHODS

During the study, 60 women aged 14 to 50 years with endometrial hyperplastic processes were examined. The average body weight of the patients was 65 kilograms. Two groups were formed: the second group served as the control group and comprised 30 women, also aged 14 to 50 years and weighing approximately 65 kg. The inclusion criteria were the presence of diagnosed hyperplastic changes in the endometrium, absence of malignant neoplasms, and informed consent to participate in the study. The exclusion criteria included severe somatic diseases, pregnancy, oncological pathology, and refusal to participate. The control group consisted of women without gynaecological pathology.

All participants underwent a detailed collection of gynaecological, reproductive, and somatic history, as well as clinical, laboratory, and instrumental examinations. The study was conducted at the Zaporizhzhia Medical Academy of Postgraduate Education of the Ministry of Health of Ukraine, from 1 June 2023 to 1 June 2024. All participants signed informed consent forms, which outlined the purpose, methods, and potential risks of the study, and guaranteed confidentiality of personal data and medical results.

The study was conducted in accordance with the ethical standards of the Declaration of Helsinki and was approved by the local ethics committee [10]. Specifically, information was gathered on the regularity of the menstrual cycle, the presence of pathological bleeding such as menorrhagia or intermenstrual bleeding, and a history of gynaecological diseases, including chronic inflammatory processes of the pelvic organs, endometrial polyps, and uterine fibroids. This information was obtained through patient interviews during the study.

Additionally, data were collected on previous pregnancies, childbirths, abortions and any related complications, the use of contraceptives and their effect on the menstrual cycle. Reproductive history included assessment of the number of pregnancies, deliveries, and abortions, as well as potential fertility issues or miscarriages, and the use of ovulation-stimulating medications. The presence of syndromes that could affect reproductive function, such as polycystic ovary syndrome, was also assessed. The somatic history enabled the collection of information regarding chronic diseases such as hypertension, diabetes mellitus, cardiovascular conditions, hepatic and renal disorders, as well as the presence of endocrine abnormalities, particularly hypothyroidism or autoimmune thyroid diseases. Data concerning body weight, obesity, and lifestyle factors – including nutrition, physical activity, and harmful habits such as smoking or alcohol consumption – were also recorded. In addition, the patients underwent a clinical examination, which included a general physical assessment, blood pressure measurement, and evaluation of the genital organs via gynaecological examination, abdominal palpation, and cervical inspection.

Laboratory testing was conducted once, in the early morning hours (07:00-08:00), on an empty stomach, taking into account diurnal hormonal fluctuations. Levels of thyroid-stimulating hormone (TSH), triiodothyronine (T3), thyroxine (T4), and antibodies to thyroid peroxidase, as well as oestrogens, progesterone, follicle-stimulating hormone (FSH), and luteinising hormone (LH), were measured using enzyme-linked immunosorbent assay (ELISA) and chemiluminescent immunoassay on the Cobas e411 automatic analyser (Roche Diagnostics, Switzerland).

A complete blood count and urinalysis were carried out using haematological and automatic biochemical analysers, respectively. Blood glucose levels were determined using the glucose oxidase reaction method. To detect potential infectious agents influencing endometrial status, bacteriological cultures and cytological smear examinations were performed. Instrumental diagnostics included pelvic ultrasound to assess the condition of the uterus and ovaries, and to identify any tumorous formations or anomalies. For more detailed endometrial assessment, hysteroscopy was employed, and where necessary, endometrial biopsy was performed for histological tissue analysis. This comprehensive approach enabled evaluation not only of gynaecological status but also of thyroid function, and facilitated the detection of comorbidities potentially influencing the course of endometrial hyperplastic processes. Morphological findings were interpreted according to the World Health Organization (WHO) classification [11].

The detection of antibodies to thyroid peroxidase suggested a possible autoimmune origin of the disorders, which is particularly relevant in patients with gynaecological pathology. Measurement of thyroglobulin levels further contributed to the evaluation of thyroid function and structure, especially when destructive thyroid processes were suspected. This methodology allowed for the identification of both hypo- and hyperthyroid states, which is essential for understanding the role of thyroid dysfunction in the development of endometrial proliferative processes. Statistical data analysis was performed using variational statistics in the Excel software package. Differences were considered statistically significant at $p < 0.05$. Descriptive statistics, expressed as mean ± standard deviation, were applied to characterise both parametric and non-parametric data appropriately.

RESULTS AND DISCUSSION

During the survey, it was established that the vast majority of patients – 90% – resided in urban areas, and approximately half (53.33%) were employed in the service sector or engaged in intellectual work (i.e. white-collar occupations) (Fig. 1). Only one patient (3.33%) reported exposure to occupational hazards in the workplace.

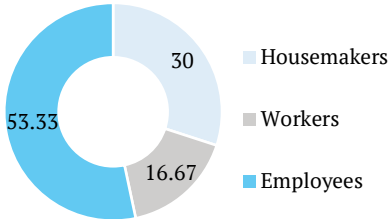

Figure 1. Distribution of examined patients by employment status
Source: created by the authors

Based on the data presented in Figure 1, it can be noted that the majority of women were white-collar workers, indicating a predominance of individuals engaged in sedentary or office-based occupations. Housewives and those involved in physical or other forms of active labour comprised a smaller proportion. This distribution may be relevant when analysing risk factors associated with lifestyle and levels of physical activity. Analysis of menstrual function revealed that the average age at menarche among patients was 12.27 ± 1.04 years. At the time of examination, only 4 women (13.33%) had regular menstrual cycles, while the majority of patients (80%) experienced heavy menstrual bleeding. Within the gynaecological history of women with endometrial hyperplastic processes, the most frequently associated diagnosis was uterine leiomyoma, observed in 63.33% of cases (Fig. 2).

Figure 2 illustrated the structure of concomitant gynaecological diseases in women with endometrial hyperplastic processes. The most prevalent pathology was salpingo-oophoritis, diagnosed in over 30% of cases. This was followed in frequency by endometrial hyperplasia, adenomyosis, cervical or uterine corpus pathology, and dysfunctional uterine bleeding. Ovarian cysts were less commonly observed. These findings highlighted a high incidence of chronic inflammatory and proliferative changes within the reproductive system among the study group. It is noteworthy that the average duration of uterine leiomyoma in

patients was 3.61 ± 0.75 years, while endometrial hyperplasia had been diagnosed in five women approximately three years prior to the current assessment. Menometrorrhagia (prolonged and heavy menstrual bleeding) was reported to have begun, on average, 2.32 ± 0.16 years before the study (range: 0.5 to 8 years). The most frequently performed surgical intervention on the reproductive system among those examined was separate diagnostic curettage of the uterine cavity, which had been undertaken in 23.33% of women. Two patients had previously undergone adnexectomy, and one had undergone cystectomy. J.G. Kruthica *et al.* [12] identified in their study that mutations in the MED12, HMGA2, COL4A5, FN1, TGFB3, and KLF6 genes were associated with the formation of leiomyomas. Among these, mutations in the MED12 gene were found to be the most common cause of leiomyomas across different populations.

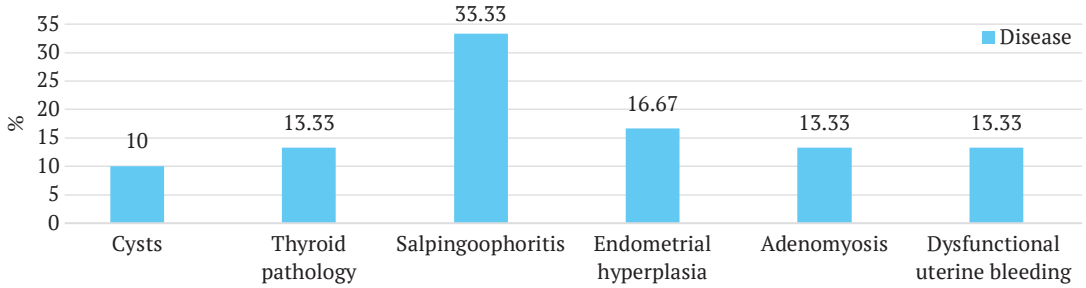

Figure 2. Prevalence of gynecological pathologies in the history of examined women
Source: created by the authors

The results of the histological examination of the removed endometrium are presented in Figure 3. The most frequent morphological form identified was simple atypical endometrial hyperplasia, which was diagnosed in 19 women. In six cases, an endometrial sample could not be obtained, most likely due to the prolonged nature of the bleeding, which resulted in either the absence or significant thinning of the uterine mucosa, rendering morphological analysis unfeasible.

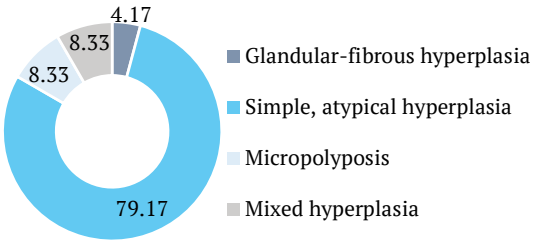

Figure 3. Structure of the results of histological examination of the endometrium
Source: created by the authors

Half of the examined women (15 individuals) had a history of childbirth, while every fourth participant (8 women or 26.67%) reported having undergone a medical termination of pregnancy. Spontaneous abortions were noted in 5 women (16.67%). The average number of pregnancies was 1.58 ± 0.14, deliveries – 1.24 ± 0.22, and abortions – 1.29 ± 0.09. It is notable that the maximum number of deliveries did not exceed two, induced abortions – three, and spontaneous abortions – one. Within the structure of somatic pathology, arterial hypertension was the most frequently observed condition, recorded in 4 women (13.33%). Isolated cases of diabetes mellitus, liver disease, and renal disorders were also noted. A history of thyroid pathology was found in 12 women (40%), of whom half (6 patients, or 20% of the total cohort) had hypothyroidism. Thyroid nodules were identified in 5 women (16.67%), one woman had thyrotoxicosis, and another had undergone bilateral thyroid lobe resection. The average duration of thyroid disease was 7.46 ± 1.03 years.

Ultrasound examination of the thyroid gland revealed no abnormalities in only one patient. Nodular formations were visualised in 15 women (50%), diffuse parenchymal changes in 8 women (26.67%), follicular formations in 2 cases, and isolated cases of hyperplasia, thyroiditis, atrophy, or post-resection changes were also observed. The average volume of the thyroid gland was 10.78 ± 1.05 cm^3, with the right lobe measuring 6.57 ± 0.24 cm^3 and the left lobe 6.31 ± 0.17 cm^3. The average volume of the nodules was 0.86 ± 0.04 cm^3. Ultrasound measurements of the uterus and ovaries were consistent with age-related norms. However, the M-echo thickness on days 5-7 of the menstrual cycle was 10.06 ± 1.17 mm (range: 3.2 mm to 18.5 mm), exceeding physiological parameters and suggesting the presence of endometrial hyperplasia. Thyroid function assessment revealed the following hormone levels: thyroid-stimulating hormone (TSH) – 3.55 mIU/L, free thyroxine (T4) – 16.03 pmol/L, triiodothyronine (T3) – 3.94 pmol/L, antibodies to thyroid peroxidase – 97.28 IU/mL, and thyroglobulin – 21.72 ng/mL. These findings indicate that the TSH level approached the upper limit of the normal range, T3 was below normal, while other indicators remained within reference values.

During the study, it was found that 60% of patients with endometrial pathology had thyroid dysfunction. Subclinical hypothyroidism was most frequently diagnosed, accounting for 20% of cases, while clinical hypothyroidism and thyrotoxicosis were each observed in 10% of cases. Additionally, a euthyroid state with elevated antibodies to thyroid peroxidase was recorded in 20% of patients, indicating autoimmune thyroid pathology without overt clinical manifestations. A. Muzafar Jafaar & M.Q. Meena [13] reported that most cases of hypothyroidism in their study were attributable to autoimmune thyroid disease, supported by the presence of goitre and elevated levels of both anti-thyroid antibodies.

Analysis of the types of endometrial pathology revealed that the highest proportion of patients with thyroid dysfunction had endometrial hyperplasia – comprising 40% of the cohort. Among these, 70% had coexisting thyroid dysfunction. In the subgroup with endometrial polyps, thyroid dysfunction was identified in 50% of cases. In patients with atypical hyperplasia, observed in three individuals, the incidence of thyroid pathology reached 30%, suggesting a potential impact of thyroid hormone imbalance on the development of more severe forms of endometrial hyperplasia. The relationship between thyroid-stimulating hormone (TSH) levels and endometrial thickness was also examined. In patients with elevated TSH levels (above 4 mIU/L), the average endometrial thickness was 12.3 ± 2.1 mm, compared to 9.6 ± 1.7 mm in those with normal TSH levels ($p < 0.01$). This finding suggests a possible role of hypothyroidism in promoting proliferative changes in the endometrium. B. Gautam *et al.* [14] analysed patients who tested positive for anti-TPO antibodies, including 59 women. A significant positive correlation was observed between TSH and anti-TPO levels, along with a negative correlation between free T3, T4 and anti-TPO. These findings underscore the value of anti-TPO level determination for the early detection and confirmation of autoimmune thyroid disease.Elevated levels of antibodies to thyroid peroxidase were found in 30% of the total cohort. Among these, 60% also exhibited menstrual irregularities, such as anovulatory bleeding or secondary amenorrhoea. This further supports the association between autoimmune thyroiditis and disrupted endometrial function.

Ultrasound examination of the thyroid gland revealed structural changes in 40% of the participants. The most common findings included signs of diffuse thyroiditis and the presence of nodules (20%). Nodular goitre was more frequently observed in patients with endometrial polyps, whereas diffuse changes predominated in the group with endometrial hyperplasia. Additionally, among women with elevated thyroid-stimulating hormone (TSH) levels and reduced concentrations of free T4, 80% reported symptoms such as excess weight, increased fatigue, and dry skin, indicating the systemic nature of hypothyroidism. In this subgroup, delayed menstruation (60%) and anovulation were also more common, suggesting that these endocrine disturbances may have contributed to the structural changes in the endometrium. Particular attention was given to patients with recurrent endometrial hyperplasia following hormonal therapy. In 60% of these cases, previously undiagnosed or latent hypothyroidism was identified. This finding suggests that untreated thyroid dysfunction may reduce the effectiveness of treatment for endometrial pathologies. Comparison of treatment outcomes showed that patients whose thyroid function was normalised (via levothyroxine or antithyroid therapy) demonstrated better clinical outcomes, including reduced endometrial thickness, regularisation of the menstrual cycle, and a lower recurrence rate of hyperplasia. A. Nayak [15] conducted a study investigating the relationship between thyroid dysfunction and abnormal menstrual bleeding, reporting that 32.6% of participants had hypothyroidism and 2.5% had hyperthyroidism. Hypothyroidism was most common among women with menorrhagia and metrorrhagia, as well as in cases of pubertal menorrhagia. Furthermore, 17.6% of patients with endometrial hyperplasia in that study had hypothyroidism. These data underscore the importance of assessing thyroid function in women with menstrual irregularities to ensure timely diagnosis and effective treatment. A similar viewpoint is presented by R.A. Safonov *et al.* [16], who reported that significant abnormalities in steroid hormone levels in women with thyroid dysfunction support the existence of a relationship between endometrial proliferative processes and thyroid function. Their findings, like the current study, demonstrated a close association between thyroid dysfunction and abnormal uterine bleeding.

As part of this research, patients were stratified into age groups to assess the influence of age on the frequency of thyroid dysfunction in the context of endometrial pathology. The highest frequency of thyroid dysfunction was recorded in women aged 36-45 years, at 66.7% (10 out of 15). In the younger cohort (20-35 years; 9 patients), the rate was 55.6% (5 women), and among those over 45 years (6 patients), it was 50% (3 women). These results indicate a heightened vulnerability to endocrine dysregulation among women of mid-reproductive age, likely due to the combined influence of hormonal fluctuations, stress, and metabolic changes. F. Memon *et al.* [17] also noted that thyroid fibrosis was most prevalent (36%) in middle-aged patients, while the thickness of the basement membrane was lowest in younger patients (12%) and highest in older patients (31%), which supports the reliability of the present data. The relationship between body mass index (BMI) and thyroid function was also examined. Among the 19 overweight patients (BMI >25), thyroid dysfunction was observed in 73.7% (14 women). In contrast, among the 11 patients with normal weight (BMI ⩽25), only 36.4% (4 women) had thyroid dysfunction. Furthermore, of the 12 women with confirmed hypothyroidism, 83.3% (10 patients) had a BMI over 25. This finding points to a close association between reduced thyroid function and metabolic disturbances, including obesity. E.M. Milewska-Kobos *et al.* [18] and F. Torre *et al.* [19] have similarly indicated a connection between increased body weight and thyroid status. Excessive obesity and adipose tissue dysfunction may contribute to the development of thyroid disorders such as autoimmunity, thyroid nodules, and thyroid cancer. The prevalence of thyroid disease is significantly higher among obese individuals than in those with normal weight, particularly in the presence of unhealthy obesity phenotypes.

Among the eight women diagnosed with autoimmune thyroiditis, three (37.5%) also exhibited ultrasound signs of polycystic ovary syndrome (PCOS). These patients experienced prolonged anovulatory cycles and menstrual irregularities, which were associated with hyperplastic processes in the endometrium. It was found that five out of eight (62.5%) patients with autoimmune thyroiditis and chronic anovulation had complex forms of endometrial hyperplasia, including cases with proliferative and atypical changes. This underscores the importance of thyroid function in regulating the endocrine axis – hypothalamus-pituitary-ovarian – and its influence on the endometrium. A retrospective analysis of reproductive history revealed that out of 30 patients, nine women (30%) had a history of miscarriage or infertility. Among these, seven (77.8%) had thyroid dysfunction, suggesting a potential role in the onset or persistence of reproductive disorders. Specifically,

three cases involved hypothyroidism, while two patients exhibited elevated titres of antibodies to thyroid peroxidase despite maintaining a euthyroid state. Such immune activity could interfere with implantation or early embryonic development. A. Beadini *et al.* [20] also identified a link between autoimmune thyroiditis and PCOS, reporting that among women with PCOS, 26.03% had markers of autoimmune thyroiditis (elevated anti-TPO or anti-Tg levels), compared to only 9.72% in the control group. This suggests a significantly higher risk of developing autoimmune thyroiditis in women with PCOS, irrespective of geographic location or diagnostic criteria. Additional analysis of clinical symptoms associated with thyroid dysfunction demonstrated a relationship with the type of endometrial changes. Among the 12 patients with hypothyroidism, the most commonly reported symptoms were fatigue (83.3%, 10 women), facial or limb swelling (58.3%, 7 women), dry skin (66.7%, 8 women), and menstrual irregularities (91.7%, 11 women). In contrast, among the 12 patients without thyroid pathology, these symptoms were significantly less frequent: fatigue (33.3%), swelling (16.7%), dry skin (25%), and menstrual irregularities (41.7%). Statistical analysis confirmed a significant difference in the prevalence of these symptoms between the two groups ($p < 0.05$), highlighting the clinical relevance of thyroid dysfunction in the development of endometrial disorders. Evaluation of the relationship between thyroid-stimulating hormone (TSH) levels and the type of endometrial pathology revealed that the highest mean TSH values were observed in patients with atypical hyperplasia (5.1 ± 1.3 mIU/L). In those with simple hyperplasia, the average TSH level was 4.2 ± 1.1 mIU/L, while patients with polyps had a mean TSH of 3.4 ± 1.2 mIU/L. By comparison, women without thyroid pathology had a significantly lower mean TSH level of 2.1 ± 0.7 mIU/L. These findings suggest a potential progression of endometrial pathology with increasing thyroid dysfunction. S.S. Bahreiny *et al.* [21] similarly reported that in women with abnormal uterine bleeding, the most common histopathological findings included proliferative endometrium, hyperplasia without atypia, and secretory endometrium. Hyperplastic endometrial changes were more prevalent in patients with hypothyroidism, further supporting the role of thyroid dysfunction in endometrial pathology. Additionally, endometrial thickness as measured by ultrasound was found to correlate with histopathological findings: patients diagnosed with endometrial hyperplasia had greater endometrial thickness than those in other groups.

The study analysed the effect of thyroid gland treatment on the endometrium. Among six patients who received levothyroxine replacement therapy for hypothyroidism for at least six months, four (66.7%) demonstrated positive dynamics – namely, a decrease in endometrial thickness (by an average of 2.4 mm), normalisation of the menstrual cycle, and the disappearance or reduction of menorrhagia. These findings indicate the effectiveness of correcting thyroid insufficiency as a key component in the management of concomitant gynaecological pathology. Another important aspect was the assessment of free T4 levels in relation to endometrial pathology. Patients with atypical hyperplasia had statistically lower free T4 levels than those in other groups – 9.7 ± 1.4 pmol/L compared to 12.2 ± 1.5 pmol/L in women with endometrial polyps. This correlation may reflect the duration and severity of hypothyroidism as a contributing factor in the progression of endometrial pathology. The level of prolactin was also measured separately in patients with menstrual disorders and concurrent hypothyroidism. In six out of twelve such women (50%), a moderate increase in prolactin levels was detected (mean value – 33.4 ± 4.5 ng/mL). This was likely due to the stimulatory effect of elevated thyroid-stimulating hormone on prolactin production, which could negatively impact ovulatory function and contribute to chronic anovulation. The overall analysis of the study findings enabled the identification of the most significant risk factors for the development of thyroid dysfunction in women with endometrial pathology. More detailed information is presented in Table 1.

Table 1. Risk factors for thyroid pathology

Risk factor	Frequency of occurrence	Note
Overweight (BMI>25 kg/m^2)	63.6%	Mostly associated with hypothyroidism
Age 36-45 years	66.7%	The highest incidence of thyroid dysfunction
Atypical or recurrent endometrial hyperplasia	75%	Accompanied by thyroid dysfunction
Autoimmune thyroiditis	80%	Often accompanied by menstrual irregularities
Reproductive losses (miscarriage, infertility, premature birth, fetal growth retardation)	77.8%	In most cases – hypothyroidism or antibodies to thyroid peroxidase

Source: created by the authors

In order to further analyse the relationship between the functional state of the thyroid gland and the morphological structure of the endometrium, the results of histological examination were assessed. In patients with hypothyroidism, proliferative changes predominated: simple or complex hyperplasia without atypia was identified in 66.7% (8 out of 12) of cases, and atypical hyperplasia in 25% (3 women). In only one case (8.3%) was secretory endometrium observed without pathological changes. In the group of women with normal thyroid function, pathological changes were less pronounced: endometrial hyperplasia was detected in 33.3% of cases (4 out of 12), and no atypical changes were observed. Furthermore, based on the evaluation of the morphofunctional state of the endometrium in patients with varying levels of thyroid-stimulating hormone (TSH), it was noted that the higher the TSH level, the greater the likelihood of persistent endometrial thickening, regardless of the phase of the menstrual cycle. In 70% of patients with TSH >4.5 mIU/L, an endometrial thickness exceeding 11 mm was recorded, which is considered a pathological indicator for women of reproductive age, particularly in the luteal phase. In contrast, among

patients with TSH <2.5 mIU/L, such thickness was observed in only 16.7% of cases. These findings suggest that disruption of thyroid homeostasis may lead to increased stimulation of endometrial growth, potentially due to altered levels of gonadotropins or the influence of thyroid hormones on the oestrogen-progesterone balance. In this context, it is important to highlight that the study found a statistically significant correlation between TSH levels and the frequency of hyperplastic processes in the endometrium.

Another important clinical consideration was the investigation of anaemic syndrome in patients with concurrent endometrial and thyroid pathology. In nine women (30% of the sample), haemoglobin levels were below 110 g/L; in all these cases, both heavy menstrual bleeding and concomitant hypothyroidism or thyroiditis were present. This supports the hypothesis of an indirect effect of hypothyroidism on the intensity of uterine bleeding, possibly via destabilisation of the endometrial layer. An additional examination of inflammatory markers, particularly C-reactive protein (CRP), revealed that among patients with autoimmune thyroid changes (elevated anti-thyroid peroxidase antibodies), CRP levels were raised in 54.5% of cases (6 out of 11), indicating possible systemic immune activation. This finding suggests a potential role for immune mechanisms in the pathogenesis of endometrial changes, especially in the context of autoimmune thyroiditis as a systemic condition. Analysis of lifestyle and associated factors demonstrated that 10 patients (33.3%) experienced chronic stress or psycho-emotional exhaustion. Within this subgroup, thyroid pathology was identified in 70% of cases (7 women).

It was also recorded that six patients (20%) were taking combined oral contraceptives at the time of examination. Among them, only one woman was diagnosed with hypothyroidism, while the remainder had thyroid function within normal limits. This provided grounds to assume that hormonal contraception may stabilise the hormonal background to some extent, but does not influence autoimmune processes. It should also be noted that comorbid pathology was identified in five patients: arterial hypertension (three cases) and insulin resistance (two cases). All these women had concomitant hypothyroidism, suggesting the presence of a general metabolic syndrome in which thyroid insufficiency plays a significant role. Thus, the results obtained demonstrate the multifactorial influence of the thyroid gland on the condition of the endometrium. Dysfunction of this organ is associated not only with morphological changes in the endometrium, but also with general somatic and metabolic disorders, significantly complicating the clinical picture. This once again highlights the need for an individualised approach to the examination and treatment of such patients, with mandatory consideration of thyroid status in each case. H.D. Sahu *et al.* [22] analysed the relationship between hormonal oral contraceptives and thyroid function. Oral contraceptives containing oestrogens increase the level of thyroxine-binding globulin, which leads to a rise in the total serum levels of T4 and T3, while the levels of free hormones remain stable. This may complicate the interpretation of thyroid function test results, especially in women receiving levothyroxine replacement therapy, as an increase in thyroxine-binding globulin may reduce the bioavailability of free T4, necessitating an adjustment in the levothyroxine dose. In addition, in women with subclinical hypothyroidism or those on levothyroxine therapy, oral contraceptives may increase the risk of thromboembolic and cardiovascular complications. Therefore, when prescribing oral contraceptives to women with thyroid dysfunction, it is essential to consider potential changes in the hormonal profile and adjust therapy accordingly.

The investigation into the relationship between the level of antibodies to thyroid peroxidase and the type of endometrial pathology deserves particular attention. Antibodies to thyroid peroxidase were detected in 11 patients (36.7%), of whom nine had morphologically confirmed endometrial hyperplasia (81.8%). In five cases (45.5%), the hyperplasia was atypical, indicating the potential role of autoimmune inflammation in the development of proliferative processes in the endometrium. Notably, atypical hyperplasia was not observed in women without elevated levels of antibodies to thyroid peroxidase. This pattern suggests that autoimmune processes in the thyroid gland may exert systemic effects and contribute to destructive changes in the endometrium. The study also assessed the influence of reproductive history on the likelihood of developing thyroid dysfunction. Among infertile patients (six women), hypothyroidism of varying degrees or elevated antibodies to thyroid peroxidase were identified in five cases (83.3%). All these women also exhibited hyperplastic changes in the endometrium, further supporting the hypothesis that thyroid dysfunction is involved in impaired implantation processes and the development of chronic anovulation. By contrast, among patients with at least one previous normal pregnancy, thyroid pathology was detected in only 33.3% of cases (six out of 18 women). A. Muzafar Jafaar & M.Q. Meena [13] demonstrated in their study that most cases of hypothyroidism are associated with autoimmune processes, as evidenced by the high frequency of Anti-TPO and Anti-Tg antibodies and the presence of goitre in patients. These findings underscore the importance of accounting for the autoimmune component in the diagnosis and treatment of hypothyroidism. Similarly, a study by I. Upadhyay *et al.* [23] found that most patients with thyroid disease tested positive for thyroid peroxidase antibodies, confirming the autoimmune nature of these conditions. The detection of diffuse hypoechogenicity on ultrasound closely correlated with the presence of Anti-TPO antibodies, highlighting the value of ultrasound diagnostics as a non-invasive, safe, and cost-effective method for the detection and prognosis of autoimmune thyroid diseases.

The influence of seasonal factors was also examined. Among the 30 patients assessed, 18 were evaluated during the autumn-winter period. Of these, 11 women (61.1%) exhibited signs of thyroid dysfunction, compared to 6 of 12 patients (50%) examined in the spring-summer period. Although the difference was not statistically significant, it may suggest seasonal fluctuations in thyroid function, particularly in regions characterised by low insolation or iodine deficiency. In several cases (three patients), hypothyroidism was found in combination with other autoimmune conditions – specifically, one case of rheumatoid arthritis and two cases of subclinical gastritis with positive antibodies to parietal cells. These findings support the systemic nature of the autoimmune process, which extends beyond the thyroid gland and may potentially result in multiorgan involvement, including disruption of

endometrial structure. Overall, the detection rate of subclinical hypothyroidism was slightly higher (13.3%) than that of clinical hypothyroidism (10%), reinforcing the importance of screening for thyroid function even in the absence of overt symptoms. Most patients with subclinical hypothyroidism had elevated thyroid-stimulating hormone (TSH) levels with normal free T4 levels; however, even at this stage, they already presented with menstrual irregularities, increased endometrial thickness, and a heightened risk of hyperplastic processes. A comprehensive evaluation of the effectiveness of an interdisciplinary approach to managing patients with endometrial pathology and concurrent thyroid dysfunction was undertaken. It was found that, when an endocrinologist participated in correcting thyroid status, positive outcomes were achieved in 10 out of 13 such cases (76.9%), both in terms of reproductive function (normalisation of the menstrual cycle, onset of ovulation) and in the morphological condition of the endometrium (reduction in hyperplasia, regression of polyps). A.S. Vishen *et al.* [24] also determined that seasonal changes affect the histochemical properties of the thyroid gland. Specifically, during winter, the gland demonstrates increased functional activity, possibly as an adaptive response to decreased ambient temperature. I. Domuschiev [25], in studying the impact of global warming on the thyroid gland, found that elevated ambient temperatures may lead to hormonal imbalance, increasing the risk of thyroid disease. Climate change may also affect the availability of iodine in food, which is crucial for thyroid hormone synthesis.

Another significant area of investigation was the impact of body weight and body mass index (BMI) on the functional state of the thyroid gland and the nature of endometrial pathology. Among the 30 patients, 16 women (53.3%) were overweight or obese (BMI >25 kg/m^2), of whom 11 (68.8%) exhibited signs of thyroid dysfunction, primarily subclinical or overt hypothyroidism. Conversely, among women with normal body weight (14 individuals), thyroid dysfunction was detected in only 4 cases (28.6%). This disparity indicates a strong association between metabolic disorders and thyroid function. Overweight patients also more frequently exhibited hyperplastic changes in the endometrium – 75% of cases (12 out of 16) – including both simple and atypical hyperplasia. This underscores that excess body weight may act not only as an independent risk factor for endometrial hyperplasia but also as an amplifying factor in the adverse effects of thyroid dysfunction on hormonal homeostasis. An analysis of the study by S.B. Kaur *et al.* [26] confirmed that the group with elevated BMI had a greater mean endometrial thickness and a higher incidence of atypical endometrial hyperplasia. Notably, the frequency of atypical endometrial hyperplasia was significantly higher among women with increased BMI.

It is important to note that among all the examined women, 10 cases (33.3%) exhibited anovulatory or irregular menstrual cycles, and thyroid pathology was detected in 8 of these cases. In three women, the menstrual cycle exceeded 45 days, indicating a marked disruption of ovulation. Following correction of thyroid-stimulating hormone (TSH) levels and normalisation of T4 and T3 concentrations over a period of 3-6 months, normalisation of the menstrual cycle was achieved. In two cases, pregnancy occurred within one year following comprehensive treatment, further supporting the role of thyroid dysfunction in fertility disorders. H.I. Aliu-Ayo *et al.* [27] similarly found that menstrual disorders, such as oligomenorrhoea and amenorrhoea, were more prevalent among infertile women with thyroid dysfunction. A significant correlation was also observed between thyroid hormone levels and different types of menstrual cycles.

To assess the emotional state of the patients, a survey was conducted. In 12 women (40%), mild or moderate depressive syndrome was recorded, of whom nine exhibited signs of hypothyroidism. This finding corroborates the well-documented clinical association between thyroid insufficiency and depressive states. It also highlights the necessity of considering the psycho-emotional component in the management of such patients, particularly when planning hormone therapy. Among the 30 patients, only three women (10%) presented a normal histological picture of the endometrium despite clinical evidence of thyroid dysfunction. In these instances, it may be assumed that thyroid pathology had not yet progressed sufficiently to induce morphological changes, or that compensatory mechanisms had temporarily offset its effects. I.I. Rodrigues da Cunha *et al.* [28] demonstrated that even minor alterations in thyroid hormone levels can influence brain function and contribute to the development of depression. Specifically, thyroid dysfunction may result in reduced levels of serotonin and noradrenaline in the central nervous system, both of which are characteristic of depressive states. This finding further underscores the importance of early diagnosis and intervention, even in the presence of minimal symptoms. Similar conclusions were drawn in the studies by K. Gökçe & D. Doğan [29] and J. Fedorko *et al.* [30].

The results of ultrasound examination of the thyroid gland were also included in the analysis. Diffuse changes characteristic of thyroiditis was identified in 14 women (46.7%), including hypoechogenicity, structural heterogeneity, and increased vascularisation. Of these, 11 women had positive titres of antibodies to thyroid peroxidase, confirming the autoimmune nature of the thyroid pathology. Thyroid nodules were detected in five patients (16.7%), although only two of these were associated with hormonal activity. No cases of malignant lesions were identified. While this suggests a relatively low oncological risk within the sample, it highlights the importance of regular ultrasound monitoring in women presenting with both hyperplastic changes in the endometrium and nodular alterations in the thyroid gland. In summary, the study results confirmed not only the statistical, but also the clinical significance of thyroid dysfunction in patients with endometrial pathology. Particular attention should be given to women with hypothyroidism, positive autoimmune markers, excess body weight, and irregular menstrual cycles. These factors significantly increase the risk of developing proliferative changes in the endometrium and, in some instances, may contribute to the development of atypical forms of hyperplasia.

The ultrasound findings, when considered alongside laboratory indicators, enabled a more comprehensive characterisation of the structural and functional state of the thyroid gland in women with endometrial pathology. The observed diffuse changes, nodular formations, and signs of

autoimmune processes confirm the close interrelationship between the endocrine and reproductive systems. This diagnostic approach facilitates not only the timely identification of co-existing pathologies but also the development of individualised monitoring and treatment plans. Such an approach is particularly crucial for the prevention of hyperplastic and atypical changes in the endometrium. Thus, the findings of the study provide a foundation for the formulation of practical recommendations and evidence-based conclusions.

CONCLUSIONS

The study revealed a significant association between thyroid pathology and endometrial changes in patients with various forms of endometrial disease. Among the 30 patients included in the study, 60% were found to have thyroid dysfunction. Specifically, overt hypothyroidism was present in 10% of cases, subclinical hypothyroidism in 13.3%, and elevated levels of antibodies to thyroid peroxidase – indicative of autoimmune thyroid disease – in 36.7%. Simultaneously, 73.3% of patients were diagnosed with endometrial hyperplasia. Among these, 36.4% had simple hyperplasia without atypia, 18.2% had complex hyperplasia, and 45.5% had atypical hyperplasia, reflecting a substantial proportion of patients at increased oncological risk. This distribution of morphological types of hyperplasia is clinically significant for patient assessment and further management, particularly in the context of concomitant endocrine disorders.

Special attention should be directed toward overweight patients, as thyroid dysfunction was observed in 68.8% of such cases, and endometrial hyperplasia in 75%. An even higher prevalence of thyroid disorders – 80% – was noted in patients with anovulatory cycles. The correction of thyroid status was shown to have a beneficial effect on menstrual cycle regulation and the restoration of ovulation in some patients. In several instances, treatment led to normalisation of endometrial thickness and improved reproductive function, underscoring the importance of early diagnosis and intervention in thyroid pathology. The findings support the necessity of routine screening for thyroid function in patients with endometrial pathology. Early identification of dysfunction allows for timely intervention to prevent the progression of hyperplastic endometrial changes. Including ultrasound examination of the thyroid gland in the standard diagnostic protocol for women with endometrial disorders is both appropriate and advisable in clinical practice.

Thus, the results of this study underscore the importance of comprehensive diagnostic and therapeutic approaches in managing patients with endometrial pathology. This includes not only the treatment of endometrial abnormalities but also the correction of thyroid dysfunction, which significantly improves clinical outcomes and reproductive potential. A key strength of this study lies in the integrated analysis of morphological variants of endometrial hyperplasia alongside types of thyroid dysfunction, enabling a deeper exploration of the pathogenetic links between endocrine and gynaecological disorders. This contrasts with most previous studies, which have tended to examine these conditions in isolation. One of the primary limitations of the present study is the relatively small sample size, which affects the statistical power and limits the generalisability of the findings. Future research should aim to expand the study population, adopt a multicentre approach, and incorporate long-term dynamic observation with consideration of therapeutic interventions.

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CONFLICT OF INTEREST

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Стан щитоподібної залози у пацієнтів з патологією ендометрію

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Анотація. Метою цього дослідження було вивчення функціонального стану щитовидної залози у жінок із гіперпластичними процесами ендометрію, з огляду на зростаючий інтерес до ролі тиреоїдної дисфункції в етіопатогенезі проліферативних змін слизової оболонки матки. У дослідження було включено 30 жінок пізнього репродуктивного та перименопаузального віку, а саме 14-50 років, у яких діагностовано різні форми гіперпластичної патології ендометрію, на базі Запорізької медичної академії післядипломної освіти Міністерства охорони здоров'я України. Методологія дослідження передбачала клініко-лабораторне обстеження пацієнток, включаючи ультразвукову діагностику органів малого таза, гістологічне дослідження ендометрію, а також визначення рівнів тиреотропного гормону, вільних фракцій тироксину і трийодтироніну, антитіл до тиреоїдної пероксидази. Основні результати дослідження показали, що жінки із гіперплазією ендометрію мали супутні порушення функції щитовидної залози, серед яких спостерігався субклінічний або явний гіпотиреоз. Виявлено зростання рівня тиреотропного гормону (3,8 ± 1,2 мМО/л) у пацієнток з гіперплазією ендометрію порівняно з контрольною групою, а також збільшення концентрації антитіл до тиреоїдної пероксидази, що свідчить про автоімунний характер порушень. Аналіз отриманих даних дозволив виявити взаємозв'язок між вираженістю тиреоїдної дисфункції та морфологічним варіантом гіперпластичних змін ендометрію: у жінок з атиповою гіперплазією діагностували клінічно значимі порушення функції щитоподібної залози. Отримані результати свідчать про доцільність рутинного скринінгу тиреоїдної функції у жінок з гіперплазією ендометрію для виявлення прихованих форм тиреоїдної патології, яка може бути як фоновим, так і тригерним чинником проліферативних змін ендометрію. Таким чином, результати дослідження підтверджують важливість інтегрованого підходу до діагностики та лікування гіперпластичних процесів ендометрію з урахуванням стану щитоподібної залози та ендокринної системи вцілому

Ключові слова: тиреотропні гормони; менопауза; тиреоїдна дисфункція; антитіла до тиреоїдної пероксидази; гіперплазія тканини; репродуктивний вік