SUBCLINICAL HYPOTHYROIDISM: an individual approach to treatment and monitoring

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Abstract. Hypothyroidism is a clinical syndrome caused by a prolonged and persistent deficiency of thyroid hormones in the body or a decrease in their tissue effects. It is the most common type of functional thyroid disorder. The relevance of this topic is due to the high prevalence of hypothyroidism among both adults and adolescents. The disease can remain undetected for a long time, as it has a slow onset and is accompanied by subtle symptoms that typically go unnoticed. This literature review examines issues related to the treatment and monitoring of patients with subclinical hypothyroidism.

Keywords: subclinical hypothyroidism, thyroid gland, thyroid hormones, levothyroxine.

Introduction. Thyroid pathology is one of the most common endocrine problems worldwide, with iodine deficiency being the leading cause, affecting approximately a third of the world's population.

Thyroid hormones play a key role in regulating basal metabolism, influencing the functioning of the cardiovascular, nervous, and muscular systems, as well as other organs and tissues.

Hypothyroidism is a clinical syndrome caused by a deficiency of thyroid hormones. Subclinical hypothyroidism is characterized by elevated thyroid-stimulating hormone levels with normal free thyroxine concentrations, while the overt form is characterized by a combination of elevated TSH and decreased free T4 levels. [6]

A decrease in thyroid hormone concentrations leads to the suppression of all types of metabolism, decreased tissue oxygen utilization, slowed oxidative processes and enzyme activity, and impaired gas and heat exchange. These changes are accompanied by a slowdown in protein synthesis and catabolism and the accumulation of their breakdown products in the extravascular spaces of various organs and tissues. [5]

The prevalence of hypothyroidism remains high worldwide. In Europe, the disease incidence averages 3,050 cases per 100,000 population, while in Russia it is 446 cases per 100,000 population. In the United States, the prevalence of overt hypothyroidism reaches 0.3%, and subclinical hypothyroidism is 4.6%. In Uzbekistan, thyroid pathology ranks second or third among all disease classes, and the prevalence of hypothyroidism ranges from 7.8 to 10.1%, reaching 10–12% in certain regions, particularly in the city of Tashkent. [14]

Subclinical hypothyroidism is detected in 4–15% of the population, and is twice as common in women as in men. [10]

Each year, approximately 5% of patients progress from the latent form of the disease to overt disease. The prevalence of hypothyroidism increases with age, reaching 12–20% in women over 70 years of age. [5]

Despite the high prevalence of subclinical hypothyroidism, questions remain regarding the optimal patient management strategy: should replacement therapy be prescribed or should observation be limited? This issue is relevant to clinical practice and is the subject of this literature review.

The purpose of the work: is to examine and summarize current approaches to managing patients with subclinical hypothyroidism and evaluate indications for replacement therapy or observation.

Materials and Methods: The authors of this study reviewed and analyzed literature from the last 5-10 years of scientific papers from the search engines cyberleninka.ru, elpub, and GOOGLE ACADEMY and SCIENCE-EDUCATION using the above-mentioned keywords.

Main part. Subclinical hypothyroidism is the initial, asymptomatic stage of the disease, in which thyroid hormone levels remain normal despite a compensatory increase in TSH.

Despite its latent course and lack of symptoms, subclinical hypothyroidism can lead to complications such as arterial hypertension, cardiac arrhythmia and conduction disturbances, insulin resistance, and polyarthritis. In pregnant women, the disease can trigger miscarriage, preeclampsia, placental abruption, and premature birth. [13]

The main form of the disease is primary hypothyroidism (up to 99%), which occurs as a result of a pathological process within the thyroid gland itself. The most common cause is chronic autoimmune thyroiditis, more common in regions with sufficient iodine supply, as well as the consequences of medical interventions. As the autoimmune process progresses, gradual destruction of the thyroid parenchyma occurs. Organ function may remain intact for a long time (euthyroidism), but as the follicular epithelium deteriorates, a subclinical hypothyroidism phase develops. [6]

Secondary hypothyroidism, caused by insufficient secretion of TSH by the anterior pituitary gland or thyroliberin by the hypothalamus, is significantly less common than the primary form of the disease.

According to the literature, subclinical hypothyroidism is characterized by elevated thyroid-stimulating hormone levels from 5 to 10 μIU/ml with normal free thyroxine levels. As the term "subclinical" suggests, this condition is a laboratory diagnosis.

According to some estimates, its prevalence may reach 12–15%. Treatment of subclinical hypothyroidism remains a subject of ongoing debate, as there are currently no clear criteria regulating the initiation of hormone replacement therapy. [10]

The most common complaints of hypothyroidism include increased fatigue, drowsiness, dry skin, bradycardia, edema, hypercholesterolemia, muscle weakness, menstrual irregularities, and cognitive decline. [11]

Hypothyroidism was the first endocrine disorder for which hormone replacement therapy was introduced. Despite generally accepted treatment guidelines, studies have shown that 10–15% of patients receiving levothyroxine sodium continue to experience clinical symptoms and are dissatisfied with their therapy. In 25–40% of patients taking L-T4 for a long time, TSH levels may exceed the reference range. In

clinical practice, this often leads to an increase in the drug dosage; however, this approach is not always justified. [1;3]

Due to the wide variety of clinical manifestations and the lack of specificity of symptoms, the diagnosis of hypothyroidism is primarily based on biochemical parameters. Manifest primary hypothyroidism is defined by an elevated TSH concentration above the reference range, combined with a decrease in free thyroxine levels. Mild, or subclinical, hypothyroidism is considered an early stage of thyroid failure and is characterized by an elevated TSH with normal free T4 levels. The use of existing reference ranges for TSH and free thyroxine remains controversial, as they often serve as threshold values for initiating treatment. [7]

In light of the above, the risk of thyroid dysfunction should be considered when using certain medications.

Table 1. Main Iodine-Containing Pharmaceuticals

Drug Group	Drug	Iodine Content Ioda
Antiarrhythmic	Amiodarone	75 mg/tablet
Radiocontrast Iodine-Containing	Iomeprol	350 mg/ml
Radiocontrast Iodine-Containing	Other radiocontrast iodine-containing agents for intravenous administration	140–380 mg/ml
Antiseptic	Lugol	6–8 mg/drop
Cosmetic Cellulite-Reducing Agents	Celiascene	240 mg/capsule
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According to L. Rizzo et al., the mechanisms of drug-induced hypothyroidism include inhibition of thyroid hormone synthesis and release, immune-mediated reactions, drug-induced thyroiditis, mixed mechanisms, and inhibition of TSH synthesis.

Pharmacological doses of iodine normally cause a short-term decrease in thyroid hormone production (the Wolff-Chaikoff effect). However, in patients with initially reduced thyroid reserve, these adaptive mechanisms may be disrupted, leading to the development of hypothyroidism.[6]

The study also found that therapy with tyrosine kinase inhibitors can lead to the development of transient or persistent thyroid failure. Approximately one-third of patients experience a temporary increase in TSH levels that does not require treatment, necessitating regular monitoring of thyroid function. [4]

The goals of treatment are to normalize TSH levels and eliminate clinical symptoms while preventing both undertreatment and overtreatment. However, studies show that 35–60% of patients receiving levothyroxine fail to achieve target TSH levels.

Research has shown that overtreatment can lead to the development of iatrogenic hyperthyroidism, atrial fibrillation, and osteoporosis, while undercompensation is associated with increased cardiovascular risk. [7]

Despite the lack of convincing evidence of the effectiveness of replacement therapy in preventing adverse pregnancy outcomes, most experts recommend the use of L-thyroxine, considering the balance of potential benefits and risks. Timely diagnosis and treatment of thyroid pathology help reduce the incidence of pregnancy complications and improve perinatal outcomes. [9]

In approximately 40% of cases of subclinical hypothyroidism, thyroid function can normalize spontaneously. Therefore, in the absence of clinical manifestations, scientists recommend repeating the hormonal profile after 3–6 months. At the same time, in patients with increased cardiovascular risk, timely initiation of therapy can reduce the likelihood of adverse outcomes, provided that the levothyroxine dosage is carefully monitored and biochemical euthyroidism is maintained. [8]

Parameter / Patient Group	Recommended Management	Comments / Indications
TSH 5–10 mIU/L, asymptomatic	Observation	Repeat thyroid function tests after 3–6 months; assess risk factors (cardiovascular disease, age, pregnancy)
TSH >10 mIU/L	Thyroid hormone replacement therapy	Levothyroxine therapy recommended; increased risk of progression even in the absence of symptoms
Women planning pregnancy / pregnant women	Thyroid hormone replacement therapy	L-T4 is prescribed to reduce the risk of pregnancy complications and adverse fetal outcomes
Pronounced clinical symptoms of hypothyroidism	Thyroid hormone replacement therapy	Symptoms include fatigue, bradycardia, dry skin, muscle weakness, etc.
Age ≥70 years / cardiovascular disease	Individualized approach	Low starting doses of L-T4 if indicated; careful TSH monitoring; avoidance of overtreatment
Patients with autoimmune thyroiditis	Monitoring and individualized assessment	High risk of progression; regular follow-up and laboratory monitoring
Use of	Thyroid	Tyrosine kinase inhibitors,

Parameter / Patient Group	Recommended Management	Comments / Indications
medications associated with hypothyroidism	function monitoring	iodine-conta

Conclusion. Subclinical hypothyroidism often occurs without significant symptoms and is diagnosed based on laboratory data, making patient management controversial. Given the possibility of spontaneous normalization of thyroid function and the ambiguous effectiveness of therapy, the decision to prescribe levothyroxine should be individualized, especially in pregnant women and patients with increased cardiovascular risk.

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