AMERICAN ACADEMIC PUBLISHER

INTERNATIONAL JOURNAL OF MEDICAL SCIENCES

ISSN NUMBER: 2692 - 5206 Volume 6. No 03. February ,2026

UDC 616.441-008:612.017:546.47

THE ROLE OF ZINC IN ENDOCRINE-IMMUNE REGULATION IN THYROID DYSFUNCTION

Yusupova Sh.K.,
Associate Professor, Head of the Department of Hospital Therapy and Endocrinology, Andijan State Medical Institute
Aysacheva M.O.,
Assistant Professor, Department of Normal and Pathological Physiology, Andijan Branch of Kokand University.
Madumarova M.M.,
Student, Andijan Branch of Kokand University.
Ibrokhimova G.U.,
Student, Andijan Branch of Kokand University.
Gulomov Zh.M.,
Student, Andijan Branch of Kokand University.

ABSTRACT: This review explores the role of zinc in endocrine-immune regulation with a particular focus on thyroid dysfunction. Zinc is an essential trace element involved in numerous biological processes, including hormone synthesis, immune response modulation, and antioxidant defense. In thyroid physiology, zinc contributes to the regulation of thyroid hormone production and receptor function. Deficiency of zinc has been associated with impaired immune responses, increased oxidative stress, and altered thyroid hormone metabolism, potentially contributing to conditions such as hypothyroidism and autoimmune thyroid diseases. Furthermore, zinc plays a critical role in maintaining the balance between pro-inflammatory and anti-inflammatory mechanisms. Understanding the interaction between zinc status and thyroid function may provide new perspectives for prevention and supportive treatment strategies in endocrine disorders.

Keywords: zinc; thyroid dysfunction; endocrine regulation; immune system; hypothyroidism; autoimmune thyroid disease; trace elements; oxidative stress; inflammation; hormone metabolism.

РОЛЬ ЦИНКА В ЭНДОКРИННО-ИММУННОЙ РЕГУЛЯЦИИ ПРИ ДИСФУНКЦИИ ЩИТОВИДНОЙ ЖЕЛЕЗЫ

Юсупова Ш.К.,
Доцент, заведующий кафедрой госпитальной терапии и эндокринологии, Андижанский государственный медицинский институт
Айсачева М.О.,
Ассистент, кафедры нормальной и патологической физиологии, Андижанский филиал Кокандского университета.
Мадумарова М.М.,
Студентка, Андижанский филиал Кокандского университета.
Иброхимова Г.У.,
Студент, Андижанский филиал Кокандского университета.

AMERICAN ACADEMIC PUBLISHER

INTERNATIONAL JOURNAL OF MEDICAL SCIENCES

ISSN NUMBER: 2692 - 5206 Volume 6. No 03. February ,2026

Гуломов Ж.М.,
Студент, Андижанский филиал Кокандского университета

АННОТАЦИЯ: В данном обзоре рассматривается роль цинка в эндокринно-иммунной регуляции с особым акцентом на дисфункцию щитовидной железы. Цинк — важный микроэлемент, участвующий во многих биологических процессах, включая синтез гормонов, модуляцию иммунного ответа и антиоксидантную защиту. В физиологии щитовидной железы цинк способствует регуляции выработки тиреоидных гормонов и функции рецепторов. Дефицит цинка связан с нарушением иммунного ответа, повышенным окислительным стрессом и изменением метаболизма тиреоидных гормонов, потенциально способствуя развитию таких состояний, как гипотиреоз и аутоиммунные заболевания щитовидной железы. Кроме того, цинк играет критическую роль в поддержании баланса между провоспалительными и противовоспалительными механизмами. Понимание взаимодействия между уровнем цинка и функцией щитовидной железы может открыть новые перспективы для профилактики и поддерживающей терапии эндокринных расстройств.

Ключевые слова: цинк, дисфункция щитовидной железы, эндокринная регуляция, иммунная система, гипотиреоз, аутоиммунное заболевание щитовидной железы, микроэлементы, окислительный стресс, воспаление, метаболизм гормонов.

RELEVANCE: Thyroid dysfunction remains one of the most prevalent endocrine disorders worldwide, affecting millions of individuals and significantly impacting metabolic processes, cardiovascular health, and overall quality of life. In recent years, increasing attention has been paid to the interaction between the endocrine and immune systems, particularly in the pathogenesis of autoimmune thyroid diseases such as Hashimoto's thyroiditis and Graves' disease. Against this background, the role of micronutrients, especially zinc, has become highly relevant.

Zinc is a vital trace element involved in numerous physiological processes, including immune regulation, antioxidant protection, and hormone synthesis. Its deficiency is widely observed in various populations due to inadequate nutrition, chronic diseases, and environmental factors. Emerging evidence suggests that zinc imbalance may contribute to dysregulation of thyroid hormone production and impaired immune responses, thereby exacerbating thyroid dysfunction.

The relevance of this review lies in its focus on the integrative role of zinc in endocrine-immune interactions, which remains insufficiently explored despite growing scientific interest. Understanding these mechanisms is essential for developing preventive and therapeutic strategies aimed at improving thyroid health. Moreover, considering the increasing prevalence of micronutrient deficiencies globally, identifying the clinical significance of zinc in thyroid disorders may have substantial implications for public health.

Thus, this study highlights the need for a comprehensive evaluation of zinc status in patients with thyroid dysfunction and supports further research into its potential as a modifiable factor in disease management.

MATERIALS AND METHODS: This review article was conducted using a comprehensive and systematic analysis of scientific literature focusing on the role of zinc in endocrine-immune regulation and thyroid dysfunction. Relevant studies were identified through electronic databases, including PubMed, Scopus, Web of Science, and Google Scholar. The

AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES
ISSN NUMBER: 2692 - 5206 Volume 6. No 03. February ,2026

search covered publications from 2000 to 2025 to ensure both foundational and recent evidence were included.

Keywords and combinations of terms used in the search strategy included “zinc,” “thyroid dysfunction,” “endocrine-immune interaction,” “autoimmune thyroid disease,” “hypothyroidism,” “hyperthyroidism,” “oxidative stress,” and “trace elements.” Boolean operators (AND, OR) were applied to refine the search and increase relevance. Only peer-reviewed articles published in English were considered.

Inclusion criteria comprised original research articles, clinical trials, systematic reviews, and meta-analyses investigating the relationship between zinc status and thyroid function or immune regulation. Studies focusing on human subjects were prioritized, although relevant experimental and animal studies were also included to clarify underlying mechanisms. Exclusion criteria involved duplicate publications, studies lacking sufficient methodological quality, non-peer-reviewed sources, and articles not directly related to the topic.

Data extraction was performed by reviewing abstracts and full texts to identify key findings related to zinc metabolism, thyroid hormone synthesis, immune response modulation, and oxidative stress pathways. Particular attention was given to studies addressing autoimmune thyroid conditions and micronutrient deficiencies.

The collected data were analyzed qualitatively through comparative synthesis, allowing identification of consistent patterns, contradictions, and research gaps. This approach enabled a comprehensive evaluation of current evidence and facilitated a deeper understanding of the integrative role of zinc in endocrine and immune regulation associated with thyroid dysfunction.

RESULTS AND DISCUSSION: Immunity is regulated by a complex network of immune and neuroendocrine factors, which in turn require sufficient amounts of micronutrients to ensure normal functioning of the immune system. Thyroid status has been shown to influence the immune response: hypothyroidism leads to immunosuppression [1]. Another factor closely associated with immunity is zinc. Within the physiological norm (12–16 μM), this micronutrient plays an important role in the proper functioning of the immune system [1]. In fact, its deficiency leads to a decrease in the number and activity of lymphocytes, as well as an increased susceptibility to infections and tumor development [1]. The effect of thyroid hormones and zinc deficiency on immunity is associated with a decrease in intracellular signals associated with lymphocyte activation [1]. In fact, an increasing number of signaling pathways, including T-cell activation via the T-cell receptor and the cytokine IL-2, have been found to involve zinc-dependent signals [1]. Furthermore, zinc is considered essential for normal thyroid homeostasis, and several studies have shown that zinc deficiency negatively impacts the synthesis, metabolism, and action of thyroid hormones [1]. In fact, zinc deficiency affects both thyroid hormone synthesis and the binding of triiodothyronine (T3) to thyroid hormone nuclear receptors, leading to hypothyroidism [1]. Conversely, thyroid hormones are necessary for zinc absorption, so hypothyroidism can lead to acquired zinc deficiency [1]. However, the role of this relationship in immune system function is poorly understood.

The influence of hypothalamic-pituitary-adrenal axis modulation on zinc metabolism

Hypothyroidism is associated with immunosuppression, and zinc deficiency has significant effects on both thyroid function and immunity.[2] However, the effects of hypothyroidism on zinc metabolism and its possible relationship with immune status remain unclear. Therefore, we assessed zinc levels in hypothyroid mice and compared them with zinc levels in euthyroid control mice. Analysis of serum, lymph node, and femur samples from mice showed that hypothyroidism alters zinc distribution in the body.[2] Mice receiving PTU had lower femoral and lymph node zinc levels than euthyroid control mice, but serum zinc concentrations were

AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES
ISSN NUMBER: 2692 - 5206 Volume 6. No 03. February ,2026

similar (Fig. 1a). These effects were reversible with both T3 administration and zinc supplementation (Fig. 1a). Conversely, zinc supplementation in hypothyroid mice failed to reverse the low T4 and T3 levels and high circulating TSH levels observed in hypothyroid conditions, suggesting that mineral supplementation is insufficient to restore thyroid function (Figure 1b). These results indicate that hypothyroidism results in a mild mineral deficiency characterized by decreased bone zinc content and that this deficiency affects immune-critical compartments such as lymph nodes.[2]

Effect of zinc and hormone deficiency on concanavalin A-induced T cell proliferation

Since T cell function is highly dependent on changes in zinc concentration [2.1], we analyzed the effects of zinc and hormone deficiency on T cell proliferation and viability. Thus, we assessed T cell proliferation after stimulation with concanavalin A. We used TPEN and diethylenetriaminepentaacetic acid to assess zinc deficiency, and cells were cultured in hormone-free medium to assess hormone deficiency. To assess the specific dependence of the observed effects on thyroid hormones, we used triiodothyronine replacement therapy [2.1]. Selective stimulation of T lymph node cells with Con A did not result in cell proliferation in hormone-free medium. This effect was abolished by the addition of physiological concentrations of T3, but not by the addition of zinc. Furthermore, as described previously [2.1], T3 itself enhanced Con A-dependent T cell proliferation. Furthermore, TPEN (20 μM) potently inhibited T cell proliferation. The extracellular chelator DTPA was also able to suppress the proliferative response to Con A, but, unlike TPEN, concentrations equal to or greater than 60 μM were required to observe significant differences[2.1]. The inhibitory effect of both chelators was neutralized by the addition of zinc in equimolar amounts, but not by the addition of T3. However, zinc alone at these concentrations had no effect on proliferation. To better understand the mechanism of the inhibitory effect of these drugs, we analyzed the possible induction of cellular apoptosis[2.1]. The absence of hormones in the culture medium did not affect cell apoptosis. However, the presence of zinc chelators resulted in increased T-cell apoptosis, as assessed by nuclear morphology staining with Hoechst 33258, flow cytometry of fixed Annexin V-PI-labeled cells, and analysis of active caspase 3 levels. Both TPEN and DTPA induced changes in nuclear morphology typical of apoptosis, accompanied by pronounced chromatin condensation and DNA fragmentation. In addition, under these conditions, an increase in the number of annexin V and PI-stained cells and an increase in the level of active caspase 3 were observed. All these effects were abolished by zinc supplementation[2.1].

The relationship between zinc and thyroid hormone levels

The results of one study included in this review showed a correlation between thyroid-stimulating hormone concentrations and plasma zinc levels. On the other hand, seven studies found no significant correlation between these two parameters.[3] Regarding the correlation between free thyroid hormone fractions and zinc, two of the five studies that assessed free thyroxine concentrations found an association between this hormone and zinc.[3] Serum free thyroxine concentrations were analyzed in seven studies, one of which found an association between this hormone and zinc. A correlation between thyroid-stimulating hormone concentrations and zinc was noted in one study, and three studies found a correlation between thyroid-stimulating hormone concentrations and zinc. Four studies assessed the relationship between zinc concentrations and thyroid hormone levels in people with thyroid disease. Ertek et al. [3] found a correlation between zinc concentration and free thyroxine level in people with nodular goiter, as well as a correlation between zinc level and thyroid-stimulating hormone concentration in people with autoimmune thyroid diseases. Kuriyama et al. [3] found a positive correlation between zinc and serum thyroid-stimulating hormone level in patients with untreated

AMERICAN ACADEMIC PUBLISHER
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hypothyroidism, and Yoshida et al. [3] found a negative correlation between zinc and thyroxine and triiodothyronine in patients with hyperthyroidism and primary hypothyroidism. On the other hand, Przybylik-Mazurek [3] did not find a correlation between zinc concentration and thyroid hormone levels in patients with Hashimoto's disease, papillary and follicular cancer. Six studies assessed the correlation between zinc concentrations and thyroid hormone concentrations in individuals without thyroid disease. Three of these studies found no correlation between these two parameters. Revalia et al. [3] found a positive association between zinc and thyroid hormone concentrations in individuals aged 90 to 107 years. Similarly, Meunier et al. [3] found a moderate negative correlation between TT4 levels and red blood cell zinc content in middle-aged and elderly volunteers. Jain et al. [3] found an association between zinc and decreased thyroid hormone levels in men.

Zinc (Zn) is a trace mineral that influences gene expression and cell growth and serves as a cofactor for numerous enzymes involved in various physiological processes, including the synthesis and metabolism of thyroid hormones [4]. Zinc is found in high amounts in oysters and fish, legumes, nuts, red meat, whole grains, and dairy products [4]. In the thyroid gland, zinc plays a critical role in the activity of thyroid peroxidase, an enzyme necessary for the synthesis of thyroid hormones. TPO catalyzes the iodination of thyroglobulin, the protein precursor of thyroid hormones, as well as the cross-linking of iodotyrosine residues to form T4 and T3 [4]. Experimental studies in vitro and in vivo have shown that zinc acts as an antioxidant, reducing the oxidation of macromolecules such as DNA/RNA and proteins. It also attenuates the inflammatory response by reducing the formation of reactive oxygen species (ROS) [4]. Autoimmune diseases are associated with abnormal zinc levels and can lead to impaired signal transduction, affecting the immune response, cell function, and differentiation. Zinc deficiency can weaken both the innate and adaptive immune responses. Furthermore, T-cell activation and differentiation into specific subsets (Th1, Th2, Th17, and Treg) significantly affect zinc balance [4].

Zinc deficiency can impair the function of thyroid hormone receptors, affecting their ability to effectively bind thyroid hormones and regulate gene expression, leading to disruptions in thyroid hormone signaling pathways [4], may contribute to decreased thyroid hormone synthesis, and potentially contribute to the development of hypothyroidism [4]. Many studies and systematic reviews have reported an association between zinc deficiency and hypothyroidism [4]. Acquired zinc deficiency can cause another common symptom in patients with hypothyroidism: hair loss [4]. Loss of pigment, dryness, brittleness, and hair loss occur due to zinc deficiency as a cofactor for metalloenzymes. Some researchers suggest using a zinc-rich diet to achieve a euthyroid state, which may be beneficial for alopecia [4]. However, further randomized clinical trials are needed to understand the role of zinc supplementation in combating hair loss in patients with hypothyroidism. However, data on the relationship between zinc and hyperthyroidism are limited and contradictory and require further study. Some studies have shown that zinc influences the development of papillary thyroid cancer and follicular carcinoma [4]. However, a recent Mendelian randomized trial found no such effect [4], indicating the need for further study.

Zinc deficiency is associated with thyroid enlargement in children and adults. A study of 68 school-aged children showed a positive inverse correlation between zinc concentration and thyroid size [4]. The researchers suggested that the main reason for this is the loss of zinc and impaired T3 action and its binding to the nuclear receptor [4]. Similar results were obtained in a study of adults, in whom zinc concentrations were negatively correlated with thyroid volume [4], as well as adults with nodular goiter, especially in regions with iodine deficiency [4]. In patients with low zinc levels, a positive correlation was found with autoimmune thyroid diseases [4].

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ISSN NUMBER: 2692 - 5206 Volume 6. No 03. February ,2026

However, this conclusion is questionable, as a study of differences in zinc levels in women with Hashimoto's thyroiditis and healthy control women did not reveal any differences [4], suggesting the need for further investigation of the relationship between hyperthyroidism and zinc.

CONCLUSIONS: An analysis of experimental and clinical data confirms the existence of a close bidirectional relationship between zinc, thyroid hormones, and the immune system. Immune regulation is mediated through a complex interaction of neuroendocrine and immune mechanisms, in which zinc serves as a key micronutrient necessary for the normal proliferation, differentiation, and functional activity of immune cells. Experimental models of hypothyroidism demonstrate that decreased thyroid hormone levels are accompanied by zinc redistribution within the body, decreased zinc levels in bone tissue and lymph nodes, and, consequently, impaired T-cell response. Furthermore, restoration of hormonal status (T3 replacement therapy) normalizes immune parameters more effectively than zinc alone, indicating the leading role of thyroid hormones in regulating zinc homeostasis and immune function. At the same time, zinc deficiency itself has a pronounced immunosuppressive effect: it inhibits T-cell proliferation, enhances apoptosis, and disrupts intracellular signaling, including pathways mediated by the T-cell receptor and IL-2. These processes are directly relevant to the adaptive immune response and may contribute to increased susceptibility to infections, the development of autoimmune disorders, and tumorigenesis. Systematic reviews of clinical studies confirm a relationship between zinc levels and thyroid hormone concentrations, but the results remain inconsistent. Some studies have found correlations between zinc levels and TSH, free T4, or T3, while others have found no such relationships. This may be due to differences in study design, age groups, comorbidities, and methods for assessing micronutrient status. Zinc also plays a significant role in the synthesis of thyroid hormones, participating in thyroid peroxidase activity and in the functioning of nuclear thyroid hormone receptors. Its antioxidant and anti-inflammatory properties further support thyroid homeostasis. Zinc deficiency can contribute to the development of hypothyroidism, an increase in thyroid volume, and impaired peripheral hormonal action. However, data on the role of zinc in hyperthyroidism and thyroid cancer remain contradictory. Thus, zinc is an important component of endocrine-immune regulation and is involved in maintaining both immune and thyroid function. Disruption of its homeostasis can exacerbate the manifestations of hypothyroidism and immune dysfunction, creating a pathogenetic "vicious cycle." At the same time, the available data indicate the need for further randomized clinical trials to clarify the clinical significance of zinc status correction in thyroid diseases, determine optimal dosages, and evaluate the long-term effects of zinc supplementation. A deeper understanding of the mechanisms of interaction between zinc and thyroid hormones will enable the development of more effective strategies for the prevention and treatment of endocrine-immune disorders.

Literature

1.Paulazo MA, Klecha AJ, Sterle HA, Valli E., Torti H., Cayrol MF, Barreiro Arcos ML, Cremaschi GA Hypothyroidism-related zinc deficiency leads to suppression of T lymphocyte activity. Endocrine, 2019.

2. Paulazo MA, Klecha AJ, Sterle HA, Valli E., Torti H., Cayrol MF, Barreiro Arcos ML, Cremaschi GA Hypothyroidism-related zinc deficiency leads to suppression of T lymphocyte activity. Endocrine, 2019.

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2.1 Paulazo MA, Klecha AJ, Sterle HA, Valli E., Torti H., Cayrol MF, Barreiro Arcos ML, Cremaschi GA Hypothyroidism-related zinc deficiency leads to suppression of T lymphocyte activity. Endocrine, 2019.

3. Beserra JB, Morais JBS, Severo JS, Cruz KJC, de Oliveira ARS, Henriques GS, do Nascimento Marreiro D. Relation between Zinc and Thyroid Hormones in Humans: a Systematic Review. Biological Trace Element Research, 2021.

4. Shulhai A.-M., Rotondo R., Petraroli M., Patianna V., Predieri B., Iughetti L., Esposito S., Street ME The Role of Nutrition on Thyroid Function. Nutrients, 2024.