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## **The Role of Micronutrient Supplementation in the Management of Hashimoto's Thyroiditis: A Review of Current Evidence and Potential Mechanisms of Action**

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## **Abstract**

**Introduction and objective:** Hashimoto's thyroiditis (HT), the most prevalent autoimmune disorder and a primary cause of hypothyroidism globally, leads to thyroid gland damage through lymphocyte infiltration. Pharmacological treatment of HT involves the use of levothyroxine, which in most cases must be taken for life. However, supplementation with micronutrients is often overlooked. Several studies have examined the impact of substances such as selenium, zinc, vitamin B12, and vitamin D on the course of Hashimoto's disease.

**Review methods:** Review and summary of research studies available in open-source format on Google Scholar, PubMed.

**Abbreviated description of the state of knowledge:** Supplementation with selenium, zinc, vitamin D, and B12 shows potential benefits for patients with Hashimoto's disease.

**Summary:** Regular monitoring and tailored supplementation of selenium, zinc, vitamin D, and vitamin B12 can enhance overall health and disease management. Therefore, it is worth considering the supplementation of these micronutrients in the daily routine of patients with Hashimoto's thyroiditis. However, it should be noted that these supplements do not constitute a treatment for Hashimoto's disease and their effect cannot replace the intake of levothyroxine.

**Keywords:** Hashimoto's thyroiditis; Hashimoto's disease; autoimmune thyroid disease;

## **Introduction**

### **Hashimoto's thyroiditis**

Hashimoto's disease, also known as chronic lymphocytic thyroiditis, is the most common thyroiditis and one of the most frequent causes of hypothyroidism [1]. It is an autoimmune disease characterized by the infiltration of the thyroid parenchyma by lymphocytes, atrophy of the parenchyma, and the presence of antibodies specific to thyroid antigens (anti-TPO and anti-Tg). This disease disrupts the normal functioning of the thyroid,

leading to symptoms of hypothyroidism. Studies show that 80% of the disease is caused by genetic factors, while 20% is due to environmental factors [2,3]. The disease was first described in 1912 in Berlin by a surgeon from Japan, Hakaru Hashimoto.

## **Epidemiology**

Hashimoto's disease, along with iodine deficiency, is among the most common causes of hypothyroidism worldwide [4]. In countries where iodine deficiency is not prevalent, hypothyroidism affects about 1-2% of the population [1], and in individuals aged 85-89, it can affect up to 7% [5]. Hashimoto's disease occurs more frequently in women than in men [6]. The incidence of Hashimoto's disease is approximately 0.3-1.5 per 1000 people per year [7]. About 15-25% of adult women and 5-10% of men without symptoms of hypothyroidism have high titers of antithyroid antibodies. Autopsy studies reveal lymphocytic infiltration in the thyroid gland in 20-40% of examined cases [8].

## **Etiopathogenesis**

The exact etiology of the disease is not yet known. The etiopathogenesis of the disease likely involves complex interactions between genetic, environmental, and immunological factors. Studies indicate that Hashimoto's disease often runs in families, suggesting a significant role for genetic factors. Mutations in genes related to the immune system, such as HLA-DR, CTLA-4, and PTPN22, increase the risk of developing the disease [9]. Polymorphisms in genes regulating immune response, such as genes encoding HLA class II proteins, are associated with susceptibility to autoimmune thyroid diseases [10].

One area of research into the etiology of Hashimoto's disease is its association with viral infections. Viral infections, such as Epstein-Barr virus (EBV), may initiate or exacerbate the autoimmune response to the thyroid. These viruses can cause the presentation of thyroid autoantigens to the immune system, leading to autoimmunization [11].

Both excess and deficiency of iodine can influence the development of autoimmune thyroid diseases. Excess iodine can lead to increased production of thyroid antigens, which in turn stimulates the autoimmune response [12]. The etiology of the disease is multifactorial, and environmental factors also contribute to the development of the inflammatory process.

Stress is recognized as a significant factor that can affect the development and course of Hashimoto's disease. Scientific studies show that stress can modulate the immune response and contribute to the exacerbation of autoimmunization. In a study conducted by Stojanovich and Marisavljevich, it was demonstrated that psychological stress can lead to dysregulation of the immune system, which can trigger or exacerbate autoimmunization [13].

According to studies, smoking decreases the risk of Hashimoto's disease [14]. A reduced incidence of anti-Tg, anti-TPO antibodies, and hypothyroidism has been observed in smokers [15,16]. Smoking cessation may increase the titers of anti-TPO or anti-Tg antibodies [17,18] and may also develop or exacerbate the disease [19,20]. However, the details of the protective mechanism of smoking in the course of Hashimoto's disease have not been clarified by research. The impact of alcohol consumption on chronic autoimmune thyroiditis is also the subject of many studies. Research suggests that moderate alcohol consumption may be associated with a lower risk of developing autoimmune thyroid diseases, including Hashimoto's. This mechanism may be related to the immunomodulatory effects of alcohol [21]. Moderate alcohol consumption was also associated with lower levels of anti-TPO antibodies in patients with Hashimoto's disease, suggesting that alcohol may influence the autoimmune response and reduce the severity of the disease [22].

### **Symptoms of HT**

Hashimoto's disease, through changes in the thyroid parenchyma, leads to its dysfunction, thus the symptoms of this disease are those of hypothyroidism. The symptoms are nonspecific. Thyroid hormones affect the functioning of many organs in the body. Symptoms of Hashimoto's disease can be varied and develop gradually, sometimes making diagnosis difficult.

One of the most commonly reported symptoms of hypothyroidism is fatigue and weakness [23]. Weight gain is a common symptom, resulting from the reduced metabolic rate associated with hypothyroidism [24]. Patients may experience cold intolerance due to decreased thermogenesis and a slowed metabolism [25].

Another frequent symptom of Hashimoto's disease is dry skin and hair, which results from decreased production of sebum and sweat, as well as slowed cell renewal [23]. Facial and limb swelling may occur due to the accumulation of mucopolysaccharides in the

subcutaneous tissues [24]. Psychiatric symptoms, such as depression, anxiety, and mood changes, are often associated with hypothyroidism [26].

Patients may experience memory and concentration problems, often referred to as "brain fog" [27]. Women may have irregular menstrual cycles, heavy menstrual bleeding (menorrhagia), and in some cases, absence of menstruation (amenorrhea) [28].

Additionally, other symptoms often mentioned include chronic constipation, brittle hair, a changed voice, sinus bradycardia, and even encephalopathy associated with Hashimoto's disease.

### **Diagnosis and treatment**

The diagnosis of Hashimoto's disease is established by correlating clinical features with the presence of anti-TG/anti-TPO antibodies and characteristic ultrasound findings. Sometimes, fine-needle aspiration biopsy of the thyroid parenchyma is used for diagnosis. There is no causal treatment for Hashimoto's disease. Pharmacological treatment involves the administration of levothyroxine (a synthetically produced hormone with the same action as the natural hormone produced by the thyroid). This medication is usually taken for life, and systematic administration leads to the proper functioning of organs influenced by thyroid hormones. Dosages are individualized based on the unique absorption and metabolism of the synthetic thyroid hormone.

Numerous studies have examined the impact of substances such as selenium, zinc, vitamin B12, and vitamin D on the course of Hashimoto's disease.

### **Selenium in Hashimoto's disease**

Selenium is one of the trace elements found in the human body. The primary storage site for selenium is skeletal muscles, but the thyroid has the highest concentration of selenium among all tissues in the body. Selenium deficiency inhibits the synthesis of thyroid hormones by deactivating selenoproteinases, which are responsible, among other things, for converting T4 to T3. Reduced thyroid hormone production increases TSH secretion, which in turn activates deiodinases, leading to the production of hydrogen peroxide, which causes fibrosis and damage to the thyroid parenchyma.

Food is the main source of selenium for humans. It is found in foods such as fish, meat, cereals, dairy products, cruciferous vegetables, garlic, asparagus, and lentils [29]. The selenium content in vegetables and fruits depends on the quality of the soil in which they are grown. Due to the low selenium content in Polish soils, animal products are the primary source of this element in Europe.

Studies have observed that selenium deficiency is more common in individuals with Hashimoto's disease compared to healthy individuals [30]. Research has demonstrated the beneficial effects of selenium supplementation for those with Hashimoto's disease. Selenium acts as an antioxidant, protecting thyroid cells from oxidative damage, which can be beneficial for patients with Hashimoto's [31].

Several studies have shown that selenium supplementation can lead to a reduction in anti-TPO (thyroid peroxidase antibodies) levels in patients with Hashimoto's disease [32]. Selenium supplementation also has the potential to reduce anti-TG (thyroglobulin antibodies) levels, although the evidence is more limited compared to anti-TPO [33].

Selenium supplementation may also improve patient well-being by reducing fatigue and improving mood, although these results are less conclusive [34].

A recent meta-analysis from 2024 evaluated the impact of selenium supplementation on thyroid function and related parameters in patients with Hashimoto's disease. It assessed TSH levels, anti-TPO antibodies, anti-TG antibodies, and oxidative stress markers such as malondialdehyde.

Selenium supplementation led to a significant reduction in TSH levels in patients not undergoing thyroid hormone replacement therapy (THRT). This suggests a beneficial effect of selenium on regulating thyroid function in patients with Hashimoto's disease who are not receiving THRT. A significant reduction in anti-TPO levels was observed, indicating that selenium may help reduce the autoimmune response in Hashimoto's disease, potentially decreasing disease activity. Malondialdehyde levels, an oxidative stress marker, significantly decreased, highlighting the antioxidant properties of selenium and its potential role in reducing oxidative damage in thyroid tissues.

The meta-analysis did not show significant changes in free and total thyroxine (fT4, T4) levels, free and total triiodothyronine (fT3, T3) levels, anti-TG levels, thyroid volume,



interleukin-2, and interleukin-10. This suggests that while selenium influences some aspects of thyroid function and autoimmune activity, its effects on these parameters are limited or require further research [35].

### **Zinc in Hashimoto's disease**

Zinc is another trace element in the human body that may play a positive role in thyroid function. It is mainly supplied through food sources such as beef, pork, poultry, seafood, milk, cheese, legumes, nuts, and seeds [36]. Zinc is crucial for the synthesis of thyroid hormones and the conversion of thyroxine (T4) to its active form, triiodothyronine (T3) [37]. It has immunomodulatory effects, which can help regulate the immune response, reducing the excessive immune activity directed against the thyroid [38]. Zinc is also a cofactor for antioxidant enzymes that protect thyroid cells from damage caused by free radicals [39].

Studies have shown that zinc supplementation can improve thyroid hormone levels in patients with hypothyroidism, including those with Hashimoto's disease [40]. Additionally, it has been observed that zinc can reduce the levels of anti-TPO antibodies [41].

### **Vitamin D in Hashimoto's disease**

Vitamin D is a prohormone, and its active form is calcitriol (1,25-dihydroxycholecalciferol). There are two forms of vitamin D – vitamin D3 (cholecalciferol) and vitamin D2 (ergocalciferol). Cholecalciferol is mainly synthesized in the skin after exposure to UVB radiation. It can also be obtained from foods such as fish, meat, eggs, offal, and dairy products. Ergocalciferol is produced by plants and fungi.

Due to the modern lifestyle characterized by staying indoors, spending long hours in front of computer screens, and less time spent outdoors, ensuring adequate sunlight exposure is challenging. Vitamin D deficiency is a widespread problem in Poland, affecting a significant portion of the population. Epidemiological studies estimate that vitamin D deficiency occurs in about 70-80% of Poles, and in winter months this number can rise to 90% [42].

Vitamin D modulates the immune response by inhibiting the production of pro-inflammatory cytokines (such as IL-6 and TNF- $\alpha$ ) and stimulating the production of anti-

inflammatory cytokines (such as IL-10). This action can reduce the inflammation in the thyroid typical of Hashimoto's disease [43]. Vitamin D can reduce the activity of B lymphocytes, leading to a decrease in the production of autoantibodies, such as anti-TPO (thyroid peroxidase antibodies) and anti-TG (thyroglobulin antibodies) [44].

Vitamin D also acts as an antioxidant, reducing the production of free radicals and improving the defensive capabilities of thyroid cells against oxidative stress [45]. Supplementation with vitamin D can lead to a significant reduction in anti-TPO antibody levels [46]. Some studies have shown that vitamin D supplementation can improve TSH levels and thyroid hormone levels (T3 and T4) [47].

### **Vitamin B12 in Hashimoto's disease**

Vitamin B12, also known as cobalamin, is an essential nutrient that plays a crucial role in numerous metabolic processes in the body. Vitamin B12 is vital for the production of red blood cells. A deficiency in this vitamin can lead to megaloblastic anemia, characterized by abnormally large red blood cells and their insufficient quantity [48]. Vitamin B12 is also involved in the synthesis of myelin, which surrounds and protects nerves [49]. It is necessary for DNA synthesis, which is key for proper cell division and tissue regeneration.

Vitamin B12 naturally occurs in animal products. High amounts of this vitamin can be found in beef, pork, poultry, fish such as tuna and mackerel, as well as in dairy products and eggs.

A deficiency in vitamin B12 can lead to megaloblastic anemia, which is characterized by large, abnormal red blood cells. Anemia is a common problem in patients with Hashimoto's, as autoimmune processes can also affect vitamin B12 absorption. Vitamin B12 is crucial for DNA synthesis in bone marrow cells, where red blood cells are produced [48].

Vitamin B12 is essential for the proper functioning of the nervous system, including the production of myelin, a substance that insulates nerves. Patients with Hashimoto's may experience neuropathy, which can be exacerbated by a deficiency in vitamin B12 [49].

Vitamin B12 plays a role in regulating the immune system, which is particularly important in autoimmune diseases like Hashimoto's. Vitamin B12 is involved in the

production of T cells, which are crucial for the immune response. It also helps in the production of antibodies [50].

Vitamin B12 affects homocysteine levels, a compound whose high levels can contribute to inflammation. By lowering homocysteine levels, vitamin B12 can help reduce inflammation [51].

Supplementation of vitamin B12 may be important for patients with Hashimoto's, especially those showing symptoms of deficiency. Regular monitoring of vitamin B12 levels and appropriate dietary or supplemental interventions can provide health benefits.

## **Conclusions**

Supplementation with selenium, zinc, vitamin D, and B12 shows potential benefits for patients with Hashimoto's disease. Selenium may reduce anti-TPO antibodies and oxidative stress, improving thyroid function. Zinc supports thyroid hormone synthesis and reduces immune activity against the thyroid. Vitamin D modulates the immune response, reduces inflammation, and lowers autoantibody levels. Vitamin B12 is crucial for red blood cell production and nerve function, helping to manage symptoms of anemia and neuropathy in Hashimoto's patients. Regular monitoring and tailored supplementation can enhance overall health and disease management. However, it should be noted that these supplements do not constitute a treatment for Hashimoto's disease and their effect cannot replace the intake of levothyroxine.

## **Disclosure**

### **Author's contribution**

Conceptualization: Andrzej Czajka and Adam Kucharski; Methodology: Alicja Wawrzyniak; Software: Alicja Chrościcka; Check: Sara Michalska and Kamil Gała; Formal analysis: Konrad Pilarski and Martyna Dewicka; Investigation: Paweł Lenard and Rafał Makuch; Resources: Kamil Gała; Data curation: Alicja Chrościcka; Writing - rough preparation: Adam Kucharski and Sara Michalska; Writing - review and editing: Alicja Wawrzyniak and Konrad Pilarski; Visualization: Martyna Dewicka; Supervision: Rafał Makuch; Project administration: Rafał Makuch and Paweł Lenard; Receiving funding - no specific funding.

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The authors deny any conflict of interest.

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