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## **The role of vitamin d in the prevention and treatment of autoimmune diseases – A literature review and analysis of research**

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## **Abstract**

**Introduction and purpose.** Autoimmune diseases are a group of diseases in which the immune system attacks the body's own cells, leading to chronic inflammation and tissue damage. In the pathogenesis of these diseases, dysregulation of the immune response, including excessive activity of T and B lymphocytes and macrophages, play a key role. The aim of this work is to review the role of vitamin D in the prevention and treatment of autoimmune diseases, with particular emphasis on Hashimoto's disease, rheumatoid arthritis and Crohn's disease.

**Methods.** A literature review was conducted based on the PubMed and Google Scholar databases, using the key words: "vitamin D", "Hashimoto's disease", "rheumatoid arthritis", "Crohn's disease". Articles published within the last five years were prioritized.

**Brief description of the state of knowledge.** Vitamin D affects the immune system through the presence of vitamin D receptors (VDR) on immune cells, such as T and B lymphocytes and macrophages. The active form of vitamin D (calcitriol) supports the development of regulatory T cells (Treg), which inhibit excessive inflammatory response, and reduces the activity of Th1 and Th17 lymphocytes. Vitamin D deficiency can disrupt this regulation, increasing the risk of developing autoimmune diseases.

**Conclusions.** Vitamin D plays an important role in the prevention and treatment of autoimmune diseases. It has an immunomodulatory effect, restoring the balance of the inflammatory response, which is crucial in the treatment of diseases such as Hashimoto's, rheumatoid arthritis and Crohn's disease. Vitamin D supplementation can alleviate symptoms, improve organ function and reduce the severity of autoimmune diseases.

**Keywords:** vitamin D, hashimoto's thyroiditis, rheumatoid arthritis, crohn's disease, autoimmune disease.

## **Introduction and Objective**

Autoimmune diseases constitute a group of disorders in which the immune system attacks the body's own cells, leading to tissue damage and organ dysfunction. Their pathogenesis is complex and involves interactions between genetic, environmental, and immunological

factors, resulting in the aberrant activation of the immune system. Among the most common autoimmune diseases are multiple sclerosis, type 1 diabetes, rheumatoid arthritis, and thyroid disorders, all of which significantly impact patients' health, causing chronic inflammation and impairment of various organ functions.

Research indicates that dysregulation of immune response plays a crucial role in the pathogenesis of these diseases, including excessive activity of T and B lymphocytes and the production of antibodies directed against the body's own cells [1,2].

Vitamin D is a critical nutrient that influences numerous physiological functions, including the regulation of the immune system. Its active form, calcitriol, interacts with various immune cells, such as T and B lymphocytes and macrophages, modulating both the inflammatory and immune responses [4]. Vitamin D exhibits immunomodulatory properties, which may have potential significance in the prevention and treatment of autoimmune diseases, where the immune system is excessively activated [3]. Deficiency in vitamin D is commonly observed in patients with autoimmune disorders, suggesting its role in the regulation of immune responses and in maintaining immune homeostasis [5].

In recent years, there has been an increasing body of research highlighting the beneficial effects of vitamin D supplementation in the treatment and prevention of autoimmune diseases. Growing evidence suggests that adequate levels of vitamin D may help reduce the severity of symptoms in diseases such as rheumatoid arthritis, Hashimoto's thyroiditis, and Crohn's disease, by modulating immune responses and decreasing inflammation [6]. Consequently, vitamin D supplementation is emerging as a promising therapeutic strategy, although the mechanisms underlying its action remain the subject of ongoing investigation [7].

The purpose of the beginning of the work is to review the available literature on the role of vitamin D in the prevention and treatment of selected autoimmune diseases, such as Hashimoto's thyroiditis, rheumatoid arthritis, and Crohn's disease. Vitamin D plays a crucial role in regulating immune responses, and its deficiency may contribute to the development and exacerbation of autoimmune diseases. Studies suggest a potential impact of vitamin D in modulating the inflammatory response in conditions such as rheumatoid arthritis, where supplementation may help alleviate symptoms and improve joint function [9]. Similarly, in the context of Crohn's disease, some studies indicate that vitamin D may play a role in reducing intestinal inflammation, with supplementation appearing beneficial in reducing the frequency of disease flare-ups [8]. In the case of Hashimoto's thyroiditis, an increasing number of studies highlight the association between vitamin D deficiency and the development of autoimmune thyroiditis, suggesting that vitamin D supplementation may aid in disease management and improve thyroid function [11][12]. The paper also aims to assess the effectiveness of vitamin D supplementation in the therapy and prevention of these conditions. Various studies demonstrate that replenishing vitamin D levels in patients with autoimmune diseases may lead to improvements in health status, although the results remain diverse and warrant further investigation [10].

## **Methods**

The literature review was conducted through the electronic databases PubMed and Google Scholar, using key search terms such as "vitamin D", "Hashimoto's thyroiditis", "Rheumatoid

arthritis", "Crohn's disease" and related variations. The focus was on clinical trials, double-blind randomized controlled trials, meta-analyses, systematic reviews, and other review articles, particularly those published in the past five years. Case reports were not included in the review.

## **Brief Description of the State of Knowledge**

### **3.1 Vitamin D and the immune system**

Vitamin D plays a key role in regulating the immune system. Its action on the immune system is associated with vitamin D receptors (VDR), which are found on the surface of many immune cells, such as T and B lymphocytes and macrophages. VDR receptors allow the active form of vitamin D, calcitriol, to interact with the immune system and regulate the expression of genes responsible for the immune response. Studies show that by activating VDR, vitamin D affects the differentiation and function of T and B cells, which is of great importance in controlling the body's inflammatory responses [18].

One of the most important effects of vitamin D on T lymphocytes is supporting the development of regulatory T lymphocytes (Treg), which are crucial for inhibiting excessive inflammatory reactions. Treg lymphocytes act as "guardians" of the immune response, preventing excessive stimulation of the immune system, which can lead to autoaggression and the development of autoimmune diseases. The effect of vitamin D on T lymphocytes also includes reducing the activity of pro-inflammatory Th1 and Th17 lymphocytes, which produce cytokines such as interferon-gamma (IFN- $\gamma$ ) and interleukin-17 (IL-17). These cytokines are strongly associated with the pathogenesis of many autoimmune diseases, including multiple sclerosis and rheumatoid arthritis [19].

Vitamin D also affects B lymphocytes, which are responsible for the production of antibodies. Its action limits the activity of B lymphocytes and the production of autoantibodies, which may contribute to the development of autoimmune diseases such as systemic lupus erythematosus or Hashimoto's disease. Studies show that vitamin D inhibits the uncontrolled proliferation of B lymphocytes, which reduces the risk of autoaggression and uncontrolled inflammatory reactions [20].

Macrophages, which are an important element of innate immunity, are also influenced by vitamin D. This vitamin activates macrophages, increasing their ability to eliminate pathogens and phagocytose, while limiting the production of pro-inflammatory cytokines such as TNF- $\alpha$ . Thanks to this, vitamin D supports the balance between the body's defense reactions and the limitation of inflammation, which is crucial in the prevention of inflammatory and infectious diseases [22]. Vitamin D deficiency is associated with impaired immune system function, which can lead to increased susceptibility to infections and increased inflammation. Deficiencies of this vitamin are particularly common in people with autoimmune diseases, in whom the immune response is dysregulated. In the case of low vitamin D levels, impaired Treg lymphocyte function and excessive Th1 and Th17 lymphocyte activity are observed, which can lead to overproduction of pro-inflammatory cytokines and exacerbation of the inflammatory process in the body [14,17]. The relationship between vitamin D and autoimmune diseases has become the subject of numerous studies that confirm the role of this

vitamin as a key regulator of immunity. Vitamin D deficiencies are commonly observed in patients with diseases such as type 1 diabetes, multiple sclerosis and lupus, which suggests that appropriate vitamin D supplementation may contribute to alleviating symptoms and limiting the progression of these diseases [13,15].

It is also worth paying attention to the role of vitamin D in the context of the gut microbiome, which affects the functioning of the immune system. Vitamin D deficiency can lead to dysbiosis, i.e. imbalances in the gut microbiome, which can additionally contribute to the development of autoaggression. Vitamin D supports intestinal barriers and promotes the development of beneficial bacteria, which is particularly important in maintaining immune balance and preventing autoimmune diseases [21].

To sum up, vitamin D has a multifaceted effect on the immune system, affecting T and B lymphocytes, macrophages and the gut microbiome. Its action is crucial for maintaining immune balance and preventing the development of excessive inflammatory reactions. Deficiencies of this vitamin can lead to dysregulation of the immune response and increase the risk of developing autoimmune diseases. Numerous studies confirm that vitamin D supplementation can be an effective method of supporting immune health, especially in people with reduced levels of this vitamin [16].

### **3.2 Vitamin D in the prevention of autoimmune diseases**

Vitamin D may play an important role in the prevention of autoimmune diseases such as Hashimoto's disease, rheumatoid arthritis (RA) and Crohn's disease. Its immunomodulatory effect is based on the regulation of T lymphocyte activity and cytokine production, which helps control inflammatory reactions and prevents excessive autoaggression [23].

In the context of Hashimoto's disease, vitamin D may reduce the production of autoantibodies against thyroid peroxidase (TPO) and thyroglobulin, which are key markers of this disease. Regular supplementation of vitamin D has been associated with lower levels of these autoantibodies, suggesting its potential protective role in the course of Hashimoto's disease [29,30]. Studies also indicate that vitamin D deficiency may increase the risk of developing this disease, and supplementing the deficiency may support thyroid health [12].

In the case of rheumatoid arthritis, vitamin D supports the balance between pro- and anti-inflammatory responses, influencing the activity of immune cells such as T and B lymphocytes and macrophages. It counteracts the excessive secretion of pro-inflammatory cytokines such as TNF- $\alpha$ , IL-6 and IL-17, which play a key role in the pathogenesis of RA [27,28]. Regular supplementation with vitamin D may help reduce the frequency and intensity of exacerbations of this disease and improve the quality of life of patients.

Crohn's disease, like other autoimmune diseases, is associated with low vitamin D levels, which may affect inflammatory activity in the gut. Vitamin D supports the functioning of the intestinal barrier and modulation of the immune response in the gut, which helps prevent excessive inflammation and reduces the risk of exacerbations [24]. Studies have shown that in

patients with Crohn's disease, low vitamin D levels are associated with more severe symptoms and more frequent disease relapses [25].

Vitamin D supplementation in autoimmune diseases has multiple benefits. In the case of Hashimoto's, it can lead to lower levels of autoantibodies and reduce inflammation in the thyroid gland, which has a beneficial effect on the function of this organ [30]. In rheumatoid arthritis, vitamin D can counteract the progression of the disease by reducing inflammation in the joints and improving their function, which helps reduce pain and stiffness [23]. In Crohn's disease, supplementation can support the stability of the intestinal barrier, reducing the risk of infection and improving overall intestinal immunity [26].

Studies suggest that low levels of vitamin D are common in patients with autoimmune diseases, which increases susceptibility to infections and exacerbations of symptoms. Vitamin D supplementation can act as a supportive preventive measure, reducing the risk of developing autoimmune diseases in people with genetic predispositions [28]. However, the effect of vitamin D on each disease may be different, so supplementation doses should be adjusted individually, depending on the patient's blood levels of this vitamin and the characteristics of the disease.

### **3.3 Vitamin D in the treatment of autoimmune diseases**

The results of clinical studies indicate that vitamin D supplementation can significantly reduce the symptoms of these diseases and improve the quality of life of patients. In Hashimoto's disease, vitamin D acts at the immunological level, affecting autoreactive T lymphocytes and inhibiting their ability to destroy thyroid cells, which may contribute to a decrease in the level of anti-TPO and anti-TG antibodies [29]. Vitamin D supplementation reduces the level of autoantigens and improves thyroid function in patients with Hashimoto's [30].

In the case of RA, vitamin D plays an important role in inhibiting the inflammatory response by reducing the production of proinflammatory cytokines such as IL-6 and TNF- $\alpha$ , which translates into less pain and less joint swelling [18]. Studies have noted that people with RA often have vitamin D deficiencies, which is correlated with a more aggressive course of the disease [27]. Vitamin D supplementation may reduce disease activity by reducing inflammation and improving patient mobility.

Crohn's disease also has been associated with vitamin D levels. Studies suggest that vitamin D deficiency is associated with disease flares and increased inflammatory activity in the gut [25]. Patients with higher levels of vitamin D tend to have a milder disease course and a lower risk of postoperative relapses [26]. The effect of vitamin D on Crohn's may be due to its ability to regulate the intestinal barrier and reduce the permeability of the intestinal wall, which limits access of bacterial antigens to the immune system.

Therapeutic mechanisms of vitamin D in the treatment of these diseases are broad and include modulation of the immune response. Vitamin D, through its receptors (VDR), regulates the activity of T lymphocytes and macrophages, which reduces the production of proinflammatory cytokines and increases tolerance to self-antigens. In patients with RA and Hashimoto's disease, vitamin D reduces the activity of autoreactive Th17 lymphocytes and promotes the activity of regulatory T lymphocytes (Treg), which play a key role in controlling

autoimmune reactions [28]. Additionally, vitamin D may reduce the risk of exacerbations of autoimmune diseases, which has important clinical implications. A link has been shown between low vitamin D levels and sarcopenia in patients with Crohn's disease, suggesting that vitamin D may also support muscle health in this group of patients [24]. By reducing inflammation and supporting immune function, vitamin D acts comprehensively, which brings therapeutic benefits in various health aspects.

**Table 1.** Overview of clinical studies on the role of vitamin D in the treatment and prevention of autoimmune diseases [18,20,21,23,25,26].

Authors (year)	Autoimmune disease	Study objective	Study results	Conclusions
Zheng et al. (2023)	Crohn's disease	Assessment of vitamin D levels in relation to disease activity, inflammation and nutrition	Low vitamin d levels were associated with greater disease activity and higher inflammatory markers	Vitamin d supplementation may be beneficial in controlling inflammation in patients with Crohn's disease
Yamada et al. (2021)	Crohn's disease	Vitamin d levels and risk of postoperative relapse study	Lower vitamin d levels were associated with higher risk of postoperative relapse	Maintaining adequate vitamin d levels may reduce risk of relapse after surgery
Harrison et al. (2020)	Rheumatoid arthritis (RA)	Assessing the role of vitamin d in RA and its impact on immune response	Low vitamin d levels were associated with increased RA activity and increased inflammation	Vitamin d supplementation may alleviate RA symptoms and inhibit disease progression
Athanassiou et al. (2023)	Autoimmune rheumatic diseases (including	A review of the mechanisms of vitamin d action in rheumatic	Vitamin d reduces proinflammatory cytokine	Vitamin d is a promising therapeutic support in

	rheumatoid arthritis)	diseases	levels and modulates T lymphocytes	rheumatic diseases
Zhang et al. (2021)	Hashimoto's disease	A systematic review of the effect of vitamin d on autoimmune markers	Vitamin d supplementation reduces anti-TPO and anti-TG antibodies	Vitamin d may support Hashimoto's therapy by modulating the immune response
Tang et al. (2023)	Hashimoto's	A review of the effects of vitamin d on thyroid function and autoantigen levels	Vitamin d lowers autoantigen levels and improves thyroid function in patients with hashimoto's	Vitamin d supplementation may improve thyroid function indicators in patients with hashimoto's

#### 4. Conclusions

The results of the review of available literature indicate an important role of vitamin D in the prevention and treatment of selected autoimmune diseases, such as Hashimoto's disease, rheumatoid arthritis (RA) and Crohn's disease. Vitamin D, through its immunomodulatory effect, affects the regulation of the immune response, including the functions of T and B lymphocytes and macrophages, which allows to control the inflammatory response and prevent excessive autoaggression, which is the basis of the pathogenesis of many autoimmune diseases.

In the case of Hashimoto's disease, vitamin D has the potential to reduce the levels of autoantibodies against thyroid peroxidase (TPO) and thyroglobulin (TG), which are key markers of the disease. Studies suggest that vitamin D supplementation can improve thyroid function and reduce the severity of the autoimmune inflammatory process. Vitamin D deficiency is associated with a higher risk of developing the disease and worsening its course, and supplementing its levels in patients' bodies can have a positive effect on controlling the symptoms of the disease and improving thyroid function.

In the context of rheumatoid arthritis (RA), vitamin D has a protective effect by reducing the production of pro-inflammatory cytokines such as TNF- $\alpha$ , IL-6 and IL-17, which are strongly associated with the pathogenesis of the disease. Vitamin D deficiency is often observed in patients with RA and is associated with the intensification of symptoms such as pain, joint stiffness and swelling. Vitamin D supplementation can help reduce inflammation, improve joint mobility and quality of life in patients. In addition, vitamin D can inhibit disease



progression by supporting the balance between inflammatory and anti-inflammatory responses in the immune system.

In the case of Crohn's disease, vitamin D may play an important role in stabilizing the intestinal barrier and regulating the inflammatory response in the intestines. Low levels of vitamin D are associated with increased inflammatory activity and more frequent disease relapses. Vitamin D supplementation may reduce the risk of disease flares and improve the health of patients by reducing the permeability of the intestinal barrier, which limits the access of antigens to the immune system. The results of the studies indicate the benefits of maintaining an appropriate level of vitamin D, including reducing the risk of relapses after surgery and improving overall intestinal immunity.

In summary, vitamin D plays a multifaceted role in regulating the immune system, and its supplementation is a promising therapeutic strategy for autoimmune diseases. Although the results of the studies are promising, there is a need for further, more detailed analyses of the optimal doses of vitamin D supplementation depending on the individual needs of patients and the characteristics of individual autoimmune diseases. A joint analysis of studies on the effect of vitamin D on these diseases allows for a better understanding of its therapeutic potential and indicates the need to adjust treatment depending on the level of vitamin D in the patients' bodies.

### **Disclosures**

Author's contribution:

Conceptualization: MZ, MZA

Methodology: AN, GB

Software: PN, WP, GB

Check: AN, MZ, MZA

Formal analysis: MZ, PN

Investigation: MZA, WP, GB

Resources: WP, AN

Data curation: GB, PN

Writing-rough preparation: MZ, MZA

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