



## PROSPECTS FOR PREVENTION AND PROPHYLAXIS OF TYPE 1 DIABETES MELLITUS THROUGH VITAMIN D SUPPLEMENTATION

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### ABSTRACT:

**Purpose:** To investigate the prospects for prevention of type 1 diabetes mellitus (T1DM) through vitamin D supplementation in risk groups.

**Material/Methods:** A targeted review of the scientific literature by keywords in the PubMed and Google Scholar databases, over the last 10 years and the full text of the scientific reports was performed. Clinical and epidemiological studies investigating the relationship between vitamin D levels and the risk of developing T1DM were analyzed. The research study was financed with funds from the state budget, provided through the Ministry of Education and Science (MES) to the Science Fund at the Medical University – Varna for financing the scientific activity inherent in state higher education institutions under project No. 24034 “Awareness, treatment and control in patients with type 1 diabetes mellitus of long duration”.

**Results:** The results show that vitamin D deficiency is associated with a higher incidence of T1DM, and early supplementation, even in childhood, can reduce the likelihood of developing the disease. However, the results are not unambiguous and remain controversial regarding the uniformly accepted recommended dose and duration of intake.

**Conclusion:** Despite the encouraging results, additional long-term studies are needed to establish vitamin D as an effective prophylactic agent against T1DM. Early intervention in genetically predisposed individuals may be a key element in future prevention strategies.

**Keywords:** type 1 diabetes mellitus, vitamin D supplementation, prevention, prophylaxis,

### INTRODUCTION

Vitamin D, or the so-called “sunshine vitamin,” is an essential nutrient that performs multiple functions in the human body, beyond its classical role as a regulator of bone health and calcium-phosphorus metabolism. Interest in it has grown significantly over the past decade due to the accumulation of scientific evidence and increased awareness of its role in modulating the immune response, maintaining metabolic balance, and its association with a number of chronic and autoimmune diseases, such as type 1 diabetes [1, 2]. Endogenous synthesis of vitamin D through the skin through exposure to ultraviolet light is often insufficient, especially for people living in northern latitudes or those whose lifestyle is associated with limited time outdoors [3]. This necessitates the need for additional supplementation through the intake of food sources or supplements containing vitamin D, which is considered a possible strategy for the prevention and maintenance of good general health [4].

Type 1 diabetes mellitus (T1DM) is a chronic autoimmune disease characterized by beta-cell destruction in the pancreas, requiring ongoing monitoring and insulin therapy [5]. Although the exact etiology of the disease is multifactorial and includes genetic predisposition and environmental factors, recent studies have indicated a role for vitamin D in immunomodulation and prevention of T1DM [6].

Vitamin D deficiency is a common problem worldwide, including among patients with carbohydrate disorders, bone and cardiovascular diseases, psychiatric disorders, and autoimmune diseases [7]. According to a number of studies, optimal vitamin D levels can have a positive impact on immune regulation and limit inflammatory processes associated with the destruction of beta-cells in the pancreas [8]. Some studies suggest that maintaining optimal serum 25(OH) D levels is associated with a lower risk of developing T1DM in children with a familial predisposition [9].

Vitamin D receptors (VDR) are found in various tissues and organs, including pancreatic beta cells. VDR regulates autoimmunity through various mechanisms that reduce inflammation in the pancreas and the risk of developing an autoimmune response in diseases such as

rheumatoid arthritis, multiple sclerosis, and T1D. Vitamin D supplementation has a promising effect on glycemic control, by reducing glycated hemoglobin (HbA1c) levels and improving insulin sensitivity [10]. Therefore, regular monitoring of vitamin D status in at-risk groups and, if necessary, supplementation for primary prevention is recommended. However, prospective clinical studies are needed to confirm the effectiveness and define the recommended doses and duration of administration [11].

The present review aims to explore the prospects for the prevention of T1D through vitamin D supplementation in at-risk groups as a disease prevention strategy.

#### **MATERIALS AND METHODS:**

A targeted review of the scientific literature by keywords in the PubMed and Google Scholar databases, over the last 10 years and the full text of the scientific reports was performed. The selection of studies followed predefined inclusion criteria, including clinical and epidemiological studies published within the last decade, focusing on the association between vitamin D status and the risk of developing type 1 diabetes mellitus. Clinical and epidemiological studies, systematic reviews, meta-analyses that investigate the relationship between vitamin D levels and the risk of developing type 1 diabetes were analyzed. The study was carried out under project No. 24034 of the Science Fund at the Medical University, Varna, Bulgaria.

Vitamin D is a fat-soluble, steroid hormone with two main physiologically active forms: D2 (ergocalciferol) and D3 (cholecalciferol). In humans, its synthesis begins from 7-dehydrocholesterol, which, under the influence of sunlight (ultraviolet rays), is converted into vitamin D3 or is obtained in smaller quantities through food. However, its deficiency is common in more than one billion children and adults worldwide [12]. Therefore, monitoring and maintaining it within normal limits is an essential element of modern prevention and health policy.

To reach its active form, vitamin D undergoes two successive phases of hydroxylation - the first in the liver to be activated to 25-hydroxyvitamin D [25(OH)D], the predominant circulating form of vitamin D, and the second in the kidneys, under the influence of the enzyme 1 $\alpha$ -hydroxylase, encoded by the CYP27B1 gene, where 25D is converted to 1,25-dihydroxyvitamin D (Calcitriol), the active form that binds to vitamin D receptors (transcription factor) in various tissues and organs [13]. 1, 25-dihydroxy vitamin D contributes to the proper function of the musculoskeletal system by maintaining parathyroid hormone (PTH) levels within physiological limits and reducing the risk of falls and fractures. It also contributes to the function of the immune, nervous and cardiovascular systems. Its deficiency is associated with a number of diseases such as rickets, osteoporosis, fractures [14] and with a large number of autoimmune diseases, including type 1 diabetes mellitus [15, 16, 17], multiple sclerosis, systemic lupus erythematosus (SLE) or

rheumatoid arthritis. Human studies have shown that vitamin D supplementation, especially early in life, protects against the development of type 1 diabetes [18, 19]. People with optimal vitamin D levels maintain circulating 25D levels between 75-150nmol/L (30-60 ng/mL). Levels below 50 ng/mL are associated with vitamin D deficiency.

#### **RESULTS:**

There are various studies that demonstrate the relationship between vitamin D and the development of type 1 diabetes, lower insulin release and insulin resistance. Analysis of the results of several prospective cohort studies shows that vitamin D deficiency is associated with a higher incidence of type 1 diabetes, and early supplementation, even in childhood, can reduce the likelihood of developing the disease [20]. However, the results are not clear and remain controversial regarding the uniformly accepted recommended dose and duration of intake.

A review study by Marino & Mistra demonstrates that vitamin D receptors (VDR) are located in pancreatic beta cells and supplementation with it can protect them from immune attack by regulating T-cell responses [21].

Infante et al. revealed the relationship of inflammation in the pathogenesis of type 1 diabetes (T1D) with the production of cytokines and chemokines by immune and beta cells, which leads to their dysfunction and apoptosis. An important conclusion they also reached is that hypo-vitaminosis D is very common in children with type 1 diabetes (T1D) [16], therefore, early diagnosis and treatment are of key importance, especially in the first years of life in high genetic risk groups [22].

Fritsch et al. point out the benefits and beneficial effect of adding vitamin D (Calcitriol) and omega-3 fatty acids to the Mediterranean diet in children with T1D in the early stages of the disease [23].

Additionally, Aljabri and Bokhari, in their randomized controlled trial on 80 participants with type 1 diabetes, support the idea that low vitamin D is associated with insulin resistance and beta-cell destruction, contributing to the development of T1D [24].

In a meta-analysis conducted by Li et al. Among 2703 participants, it was proven that vitamin D supplementation successfully improves serum 25(OH) D levels and insulin resistance. A particularly notable effect was observed when vitamin D was administered for a short period of time in high doses to non-obese individuals who were vitamin D deficient or had good glycemic control at baseline [25].

Similarly, Mohammadian et al. investigated vitamin D supplementation in 44 patients with type 1 diabetes aged <17 years. The results of the meta-analysis found that glycemic control (HbA1C) improved at all ages and reached values <7.8, 7.8–9.9, and >9.9 [26].

The characteristics and main findings of the analyzed studies are summarized in Table 1, highlighting the heterogeneity in study design, population, and outcomes.

**Table 1.** Characteristics and main findings of studies on vitamin D and type 1 diabetes mellitus

Author (Year)	Country	Study Design	Population (n, age)	Intervention / Exposure	Outcomes Measured	Key Results	Limitations
Marino & Mistra	Not specified	Narrative review	Not specified	Vitamin D status, VDR expression	Immune modulation	VDR expressed in pancreatic $\beta$ -cells; modulation of T-cell response	Lack of quantitative data
Infante et al.	Not specified	Review / mechanistic	Not specified (children focus)	Vitamin D deficiency	Cytokines, $\beta$ -cell function	Hypovitaminosis D common in T1DM; linked to inflammation and $\beta$ -cell apoptosis	Observational bias
Fritsch et al.	Europe (multicenter)	Observational	Children with T1DM	Vitamin D + omega-3 + diet	Disease progression	Improved early-stage metabolic outcomes	Combined intervention (not isolated effect)
Aljabri & Bokhari	Saudi Arabia	Randomized Controlled Trial	n=80, T1DM patients	Vitamin D supplementation	Insulin resistance, glycemic control	Low vitamin D associated with insulin resistance; supplementation beneficial	Small sample size
Li et al.	Not specified	Meta-analysis	n=2703	Vitamin D supplementation	25(OH)D, insulin resistance	Significant improvement, especially in deficient individuals	Heterogeneity between studies
Mohammadian et al.	Not specified	Clinical study	n=44, <17 years	Vitamin D3 supplementation	HbA1c	Improved glycemic control across all baseline HbA1c levels	Small cohort
Prospective cohort studies	Multiple	Cohort	Not specified	Vitamin D levels in early life	Incidence of T1DM	Deficiency linked to higher risk; early supplementation protective	Confounding factors

## DISCUSSION:

Strategies to preserve  $\beta$ -cell mass and/or prolong remission after the onset of T1DM by vitamin D supplementation have also been proposed as tertiary prevention of the disease. These strategies allow avoiding or delaying complications, as  $\beta$ -cell mass rapidly declines during the first 1–2 years after onset [27]. In the period 2017–2020, a randomized, placebo-controlled clinical trial was conducted to test the effectiveness of vitamin D and the preservation of residual islet beta-cell function in the “honeymoon phase” or partial clinical remission (PCR) [28].

The data obtained highlight the potential of vitamin D as part of a comprehensive preventive strategy in type 1 diabetes, especially among risk groups with a family history. However, the heterogeneity in study design, dosage, duration of supplementation, and population characteristics limits direct comparison between studies and may explain the inconsistency in reported results. At the same time, meta-analyses emphasize the importance of the correct dosage and duration of supplementation, as excessive intake carries a risk of toxicity and metabolic disorders. However, there is no consensus on the optimal serum levels of vitamin D for the prevention of autoimmune diseases, but values  $\geq$  above 75 nmol/L (30 ng/mL) are considered potentially protective [29]. Its immunomodulatory effects, including the suppression of autoaggressive T cells and the increase in regulatory T lymphocytes, provide a biological basis for the protective role of the vitamin [30]. This opens up real opportunities for the use of vitamin D as part of primary prevention strategies in individuals with a genetic predisposition to the disease.

## CONCLUSION:

A growing body of scientific evidence supports the hypothesis that vitamin D plays an important role in modulating the autoimmune processes associated with the development of type 1 diabetes. Supplementation with this vitamin, especially in children from risk groups at an early age, appears to be a promising strategy for reducing the likelihood of developing the disease. Despite the encouraging results, however, additional long-term studies are needed to confirm the role of vitamin D as an effective prophylactic agent against type 1 diabetes. Therefore, well-designed, large-scale clinical trials are needed to evaluate the long-term effect, optimal dosages, and safety of vitamin D supplementation as a means of preventing type 1 diabetes. Early screening for vitamin D deficiency in genetically predisposed individuals and its timely correction may be a key element in future prevention strategies in clinical practice.

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