Health Problems of Civilization
eISSN: 2324-0265, ISSN: 2353-6942

REVIEW PAPER

Hypervitaminosis D: an underestimated complication of supplementation

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Masłowski M, Dudziak P, Woźniak T, Filipiak Z, Wabiszczewicz Ł, Golińska M, et al. Hypervitaminosis D: an underestimated complication of supplementation. Health Prob Civil. https://doi.org/10.29316/hpc/220721

Tables: 0
Figures: 0
References: 18
Submitted: 2026 Feb 27
Accepted: 2026 Apr 16

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Abstract

Vitamin D plays a crucial role in the regulation of calcium-phosphate metabolism and the proper functioning of multiple body systems. The widespread prevalence of vitamin D deficiency has led to a significant increase in supplementation in the general population over recent years. However, this trend has been accompanied by a growing number of cases of hypervitaminosis D, primarily resulting from uncontrolled intake of high-dose vitamin D preparations. Excess vitamin D leads to disturbances in calcium homeostasis, most notably hypercalcemia, which may manifest itself in nonspecific systemic symptoms and result in serious organ complications such as nephrocalcinosis and renal failure. A major contributing factor is the widespread availability of vitamin D-containing preparations, combined with insufficient patient awareness of the potential consequences of excessive intake. Therefore, the aim of this work is to present the current state of knowledge regarding hypervitaminosis D and its significance from a public health perspective. An analysis of literature indicates that physicians play a key role in the rational management of vitamin D supplementation, identification of risk factors, and patient education. Adherence to current supplementation guidelines and regular monitoring of therapy can significantly reduce the risk of developing hypervitaminosis D.

Keywords: hypervitaminosis D, hypercalcemia, vitamin D, dietary supplements, public health

Introduction

Vitamin D is a fat-soluble vitamin obtained both through cutaneous synthesis under exposure to ultraviolet radiation and through dietary intake [1]. It plays an essential role in maintaining calcium-phosphate homeostasis, which is fundamental for the proper functioning of the musculoskeletal system [2]. Only a limited number of foods naturally contain vitamin D or are fortified with it [3]. Due to seasonal variations in skin synthesis and limited dietary sources, vitamin D supplementation has become a widespread practice.

Vitamin D also exerts physiological effects unrelated directly to calcium metabolism. It stimulates insulin production, modulates inflammatory bowel diseases, and influences myocardial contractility [2]. The increasing prevalence of vitamin D deficiency, particularly in regions with limited sunlight exposure, combined with growing public awareness of its

potential health benefits, has led to a substantial rise in the use of so-called “sunshine vitamin” supplements [4]. Concurrently, an increasing number of hypervitaminosis D cases have been observed, resulting from prolonged and uncontrolled intake of vitamin D preparations at doses exceeding recommended limits [5].

Aim of the work

The aim of this study is to summarize current knowledge regarding the pathophysiology, etiology, clinical presentation, diagnosis, and prevention of hypervitaminosis D, with particular emphasis on its relevance in the context of civilization-related health problems.

Methods

This narrative review was based on an analysis of literature concerning vitamin D and its toxicity. Three databases were initially identified as potential sources of scientific publications: PubMed, Google Scholar, and Web of Science. The literature retrieval protocol was primarily developed for the PubMed database, subsequently evaluated by the research team, and used as the primary strategy for article identification. Ultimately, all the publications included in the final bibliography were retrieved from PubMed. The literature search was conducted between December 2025 and January 2026 and covered publications from 2018 to 2025. The search included the following keywords: “hypervitaminosis D”, “vitamin D”, “dietary supplements”, “hypercalcemia”, and “public health”.

Prior to the selection stage, eligibility criteria were defined. The inclusion criteria comprised recent peer-reviewed articles published in English that addressed the pathophysiology, etiology, epidemiology, clinical manifestations, diagnosis, prevention, and public health aspects of hypervitaminosis D. Priority was given to randomized controlled trials, observational studies, systematic reviews, high-quality narrative reviews, and clinical guidelines. Case reports were considered when they provided clinically relevant evidence of vitamin D intoxication. The exclusion criteria included publications not directly related to vitamin D toxicity, abstracts without full-text availability, expert opinions, and studies with insufficient methodological description.

The titles, abstracts, and full texts of the identified publications were screened to assess their relevance to the research question and suitability for inclusion in this review. The initial database search yielded 187 records. After screening titles and abstracts and applying the predefined inclusion and exclusion criteria, 18 publications met the eligibility requirements and were included in the final analysis used to synthesize the findings of this review.

Literature review results

Pathophysiology of hypervitaminosis D

Following cutaneous synthesis or oral intake, vitamin D undergoes hydroxylation in the liver to form 25-hydroxyvitamin D (25(OH)D, calcifediol), and subsequently in the kidneys, where it is converted by 1α-hydroxylase into its biologically active form, 1,25-dihydroxyvitamin D ($1,25(OH)_2D$, calcitriol) [6]. Calcifediol is the predominant circulating form of vitamin D and is routinely measured in serum due to its relative stability compared with calcitriol [7]. The active form of vitamin D exerts its effects through vitamin D receptors (VDRs), which are present in nearly all tissues, increasing intestinal calcium absorption, enhancing bone resorption, and reducing renal calcium excretion [6,8].

Hypervitaminosis D develops as a result of excessive accumulation of vitamin D in adipose tissue, leading to disproportionate activation of calcium-phosphate metabolism. Serum 25(OH)D concentrations exceeding 100 ng/mL (250 nmol/L) are associated with an increased risk of toxicity and the development of clinical symptoms and organ complications [9].

Recommendations for vitamin D supplementation

From a public health standpoint, maintaining adequate serum vitamin D concentrations while avoiding excessive intake represents an important clinical and preventive challenge. Vitamin D exists in two principal forms that act as prohormones: cholecalciferol (vitamin D_3) and ergocalciferol (vitamin D_2) [10]. In Poland, prophylaxis and treatment regimens for vitamin D deficiency are based primarily on cholecalciferol, with calcifediol reserved for specific clinical situations. Cholecalciferol is considered the first-line agent for both prevention and treatment, whereas calcifediol is recommended as a second-line option in cases of inadequate response to cholecalciferol or when a rapid increase in serum 25(OH)D levels is required [9].

The European Food Safety Authority (EFSA) estimates the recommended daily amount of vitamin D at 15 µg/day (600 IU) for adults and children aged 1-17 years, while for infants aged 7-11 months, it is set at 10 µg/day (400 IU). These values were established assuming minimal cutaneous synthesis of vitamin D [11]. Current Polish national recommendations emphasize an individualized approach to supplementation. Infants should receive approximately 400-600 IU/day, children and adolescents 600-2,000 IU/day depending on age, body weight, and sun exposure, while adults are generally recommended to receive 1,000-2000 IU/day. In older adults, particularly those over 75 years of age, higher doses of 2,000-4,000 IU/day may be recommended throughout the year due to reduced cutaneous synthesis and age-related changes in vitamin D metabolism [9]. According to guidelines for the general population, the maximum average daily oral dose that is unlikely to cause adverse effects is 4,000 IU/day for adults [12]. These recommendations underline the importance of rational supplementation and appropriate monitoring to prevent both vitamin D deficiency and potential toxicity associated with excessive intake.

Etiology

From a public health perspective, it is essential to highlight the common causes of hypervitaminosis D. Vitamin D toxicity is usually the result of unintentional or inappropriate intake of very high doses of over-the-counter dietary supplements or pharmaceutical preparations [5]. The widespread availability of supplements in online stores and retail outlets, as well as the commercialization of unregulated products, promotes their misuse [13]. Insufficient patient awareness regarding the potential adverse effects of supplementation often leads to excessive dosing [4]. It should be emphasized that despite the important role of vitamin D in maintaining health, excessive intake does not confer additional benefits [3].

Another significant issue is the inadequate quality control of dietary supplements, in which substantial discrepancies have been identified between the actual and declared vitamin D content [3]. Studies by Lin et al. also highlight public health risks associated with the uncontrolled production of dietary supplements [14]. Furthermore, challenges related to precise vitamin D dosing also apply to food fortification processes. Studies conducted in the United States have demonstrated wide discrepancies from the declared doses, reflecting the fact that food products are not subject to the same stringent regulations as medicinal products [8].

Vitamin D toxicity may also result from prescribing errors, inappropriate dosing regimens, or pharmacy dispensing mistakes, such as issuing a preparation containing 50,000 IU intended for weekly administration for daily use instead [8]. It should be noted that vitamin D supplementation at recommended doses rarely leads to toxicity [4].

Epidemiology

Hypervitaminosis D remains a relatively rare condition; however, the number of reported cases has been steadily increasing [5,8]. Vitamin D supplementation shows a rising trend among elderly individuals, due to its well-documented beneficial effects on the musculoskeletal system and related disorders common in this age group. Consequently, older adults constitute a particularly high-risk group for the development of hypervitaminosis D [15]. A high incidence of vitamin D toxicity has also been observed in the pediatric population, especially in cases of excessive dosing or concurrent use of multiple preparations [16].

Clinical presentation

The clinical manifestations of hypervitaminosis D are nonspecific and primarily result from hypercalcemia [4]. Symptoms include neuropsychiatric manifestations such as apathy, impaired concentration, confusion, and depression, as well as gastrointestinal symptoms including recurrent vomiting, nausea, abdominal pain, and constipation. Severe toxicity may lead to cardiovascular complications such as arterial hypertension, bradycardia with first-degree atrioventricular block, or QT interval shortening on electrocardiography [5]. Renal manifestations may range from hypercalciuria and polyuria to nephrocalcinosis and renal failure [17]. The severity of symptoms varies individually and does not always correlate directly with serum 25(OH)D levels [3]. Most cases of vitamin D toxicity resolve without serious long-term consequences. In some instances, severe hypercalcemia can lead to acute kidney injury (AKI), which may require temporary renal replacement therapy [18]. This condition is frequently reversible after appropriate treatment.

Diagnosis

The diagnosis of hypervitaminosis D is based on markedly elevated serum 25(OH)D concentrations (>100 ng/mL), accompanied by hypercalcemia, hyperphosphatemia, hypercalciuria, and pronounced suppression of parathyroid hormone secretion [5,9]. A detailed

medical history regarding medication use, dietary supplements, and diet is crucial, as physical examination often provides limited diagnostic information.

Hypervitaminosis D should be differentiated from other causes of hypercalcemia, including primary, secondary, and tertiary hyperparathyroidism, malignancy-associated hypercalcemia, granulomatous diseases, and Paget's disease of bone [18].

Prevention and the role of the physician

Physicians play a central role in preventing hypervitaminosis D through rational prescribing, therapy monitoring, and patient education. Particular emphasis should be placed on informing patients about the importance of adhering to prescribed dosing regimens [18]. Tailoring supplementation schedules to patient preferences and using weekly or monthly dosing regimens may improve adherence [9]. Periodic monitoring of serum 25(OH)D levels and individualized dosing based on age, body weight, sun exposure, dietary habits, and lifestyle are recommended [9,18]. Patients at increased risk of adverse effects, particularly those with borderline or elevated baseline serum calcium or phosphate levels, require closer biochemical monitoring in order to minimize the risk of hypercalcemia and related complications [18].

Limitations

This review has several limitations that should be acknowledged. Firstly, although multiple databases were initially considered during the development of the search strategy, the final identification of articles was based primarily on publications indexed in PubMed, which is one of the most widely used biomedical databases. Secondly, only articles published in English were included, which may introduce a potential language bias. Thirdly, due to the narrative nature of this review, the process of literature selection and interpretation may be associated with a certain level of subjectivity. Finally, the included studies differed in terms of study design, population characteristics, and methodological approaches, which may limit the direct comparability of the findings presented in this review.

Conclusions

Hypervitaminosis D is an increasingly observed complication of uncontrolled supplementation. Despite the well-documented health benefits of vitamin D, excessive intake may result in serious metabolic disturbances and organ damage. This review indicates that most cases of vitamin D toxicity are associated with inappropriate dosing, prolonged use of high-dose preparations, or insufficient monitoring of serum biochemical parameters.

As interest in vitamin D supplementation continues to grow, the incidence of toxicity may increase, particularly among individuals at the extremes of the age spectrum. A major public health challenge is the widespread availability of vitamin D-containing preparations combined with insufficient patient knowledge regarding the potential consequences of excessive use. Therefore, patient education, selection of pharmaceutical products with confirmed quality, adherence to current guidelines, and regular therapy monitoring are essential in preventing vitamin D toxicity. Greater awareness among both patients and healthcare professionals, along with improved regulation of vitamin D preparations, may help reduce the risk of hypervitaminosis D while preserving the benefits of appropriate supplementation.

Disclosures and acknowledgements

The authors declare no conflicts of interest with respect to the research, authorship, and/or publication of this article.

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Artificial intelligence (AI) was not used in the creation of the manuscript.

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