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Chronic urticaria and vitamin D supplementations: a systematic review

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Abstract

Background Chronic urticaria (CU), especially chronic spontaneous urticaria (CSU), is a long-term inflammatory skin condition marked by wheals and/or angioedema lasting over six weeks. Emerging evidence suggests a link between vitamin D deficiency and immune dysregulation associated with CU. Given vitamin D's immunomodulatory and anti-inflammatory effects, this review explores the therapeutic potential of vitamin D supplementation in CU management.

Methods A systematic review was conducted in accordance with PRISMA guidelines Electronic databases (PubMed, Scopus, Web of Science, and Google Scholar) were searched using relevant keywords. Studies included were randomized controlled trials (RCTs), case–control, and observational studies assessing serum vitamin D levels or supplementation in patients with CU. Data extraction and bias assessment were independently conducted using standardized tools: the Cochrane Risk of Bias Tool and the Newcastle–Ottawa Scale.

Results Eleven studies involving 1,491 participants were included. Most studies demonstrated significantly lower serum 25(OH)D levels in patients with CU compared to healthy controls. Vitamin D supplementation, particularly in individuals with a deficiency, was associated with reductions in urticaria activity scores, symptom severity, and improved quality of life. High-dose regimens (e.g., 4,000 IU/day or 60,000 IU/week) appeared more effective. However, results varied due to heterogeneity in study design, dosage, and patient characteristics.

Conclusion Vitamin D supplementation may serve as a safe, accessible adjunct to standard CU treatment, particularly for those with confirmed deficiency. While evidence suggests potential benefits, further high-quality RCTs are needed to establish causality, optimal dosing, and long-term efficacy.

Keywords Chronic urticarial, Chronic spontaneous urticarial, Vitamin D, Vitamin D supplementation, 25(OH)D, Immunomodulation, Quality of life

Introduction

Chronic urticaria (CU) is a persistent skin disorder characterized by the spontaneous or inducible appearance of wheals, angioedema, or both, lasting for six weeks or longer. It affects approximately 0.5% to 1% of the global population and can significantly impair quality of life due to its chronic, relapsing nature and associated symptoms such as itching, swelling, and sleep disruption [1]. The underlying pathophysiology of CU is complex and not fully understood, but it is believed to involve immune dysregulation,

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autoimmunity, and the activation of mast cells and basophils 2.

Recent attention has been directed toward the role of vitamin D in immune system regulation and its potential implications in various inflammatory and autoimmune disorders, including CU [3, 4]. Vitamin D is known for its immunomodulatory, anti-inflammatory, and antimicrobial properties, suggesting a possible link between vitamin D deficiency and the exacerbation or persistence of chronic urticaria symptoms [4]. Several observational studies have reported lower serum vitamin D levels in patients with CU compared to healthy individuals, raising the question of whether vitamin D supplementation could play a therapeutic role [5].

Vitamin D influences both the innate and adaptive immune systems through multiple mechanisms. It enhances the antimicrobial functions of innate immune cells such as macrophages and neutrophils, while also promoting the production of antimicrobial peptides like cathelicidin and defensins [22]. In adaptive immunity, vitamin D suppresses the activation of pro-inflammatory Th1 and Th17 cells and promotes regulatory T-cell (Treg) responses, thereby supporting immune tolerance and reducing chronic inflammation. These immunoregulatory effects are particularly relevant in allergic and autoimmune diseases, where immune imbalance plays a central role in pathogenesis [23].

In allergic conditions such as asthma, atopic dermatitis, and allergic rhinitis, vitamin D deficiency has been associated with heightened disease activity, increased exacerbation rates, and reduced responsiveness to conventional therapies [24]. Similarly, in chronic urticaria, vitamin D may modulate mast cell stability, reduce histamine release, and attenuate inflammatory cytokine production, contributing to symptom relief. These findings have prompted growing interest in the potential therapeutic benefits of vitamin D supplementation as an adjunct to standard antihistamine treatment in CU, underscoring the need for systematic evaluation of the clinical evidence [25].

Given the increasing interest in alternative and adjunctive treatments for chronic urticaria, this systematic review aims to evaluate the existing evidence on the effectiveness of vitamin D supplementation in managing CU. By synthesizing data from clinical trials and observational studies, we seek to determine whether vitamin D has a beneficial impact on symptom control, disease duration, or quality of life in individuals suffering from this chronic condition. (Table 1).

Methods.

Study design

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Fig. 1). The aim was to evaluate the relationship between vitamin D supplementation and clinical outcomes in patients with chronic urticaria (CU), particularly chronic spontaneous urticaria (CSU). The review process followed a structured protocol for literature identification, selection, data extraction, and synthesis.

Search strategy

A comprehensive literature search was carried out using electronic databases, including PubMed, Scopus, Web of Science, and Google Scholar up to March 2025. The search employed a combination of Medical Subject Headings (MeSH) and free-text keywords such as "chronic urticaria," "chronic spontaneous urticaria," "vitamin D," "vitamin D deficiency," "25(OH)D," and "vitamin D supplementation." Boolean operators (AND, OR) were used to combine terms effectively. Additionally, reference lists of selected articles were manually searched to identify any further relevant studies.

Eligibility criteria

Studies were selected based on predefined inclusion and exclusion criteria. Inclusion criteria were as follows: (1) human studies, (2) randomized controlled trials, observational studies, or case–control studies, (3) studies involving patients with CU or CSU, (4) assessment of serum vitamin D levels and/or vitamin D supplementation, and (5) studies reporting clinical outcomes such as urticaria activity scores, symptom severity, or quality of life. Exclusion criteria included reviews, editorials, animal studies, case reports, studies without sufficient clinical outcome data, and those not published in English.

Study selection

All identified articles were imported into reference management software, and duplicates were removed. Two independent reviewers screened the titles and abstracts for relevance. Full-text versions of potentially eligible articles were then assessed in detail. Discrepancies in study selection were resolved through discussion or consultation with a third reviewer to ensure consensus.

Data extraction

Data were extracted systematically using a predesigned form. Extracted information included first author's name, year of publication, study design, total number

Table 1 Study characteristics

Author (References)	Year	Study design	No of participants	Age of participants	Gender (Male/female)	Vitamin D supplement vs control/plecabo	Baseline vitamin D status	Dose of vitamin D supplement	Types of chronic Urticaria	Clinical outcomes	Quality assessment
Andy Rorie et al. [6]	2014	Randomized Controlled Trial	N = 42			vitamin D3 supplementation		high (4,000 IU/d) or low (600 IU/d) vitamin D3 supplementation	Chronic Urticaria	High-dose vitamin D3 (4,000 IU/day) may be a safe and effective add-on for chronic urticaria	*****
Tadech Boonpiyathad et al. [7]	2014	prospective case–control study	N = 60 CSU patients and N = 40 control	39 ± 16	27/73	Vitamin D 2 supplements		20,000 IU/day of ergocalciferol (vitamin D2)	chronic spontaneous urticaria (CSU)	Lower serum 25(OH)D levels are significantly associated with CSU	*****
Roohi Rasool et al. [8]	2015	randomized case control study	N = 147 patients with CU N = 130 healthy control	patients with CU = 42·83 ± 8·52 Control = 45·12 ± 7·65	47/100	Vitamin D 3 supplement	↓ serum levels of 25 (OH)2D	60,000 IU per week	Chronic Urticaria	patients with CU have low serum 25(OH)2D, and adding vitamin D3 to antihistamines and corticosteroids enhances symptom resolution	****
Amal Ahmed Mohamed et al. [9]	2022	Randomized Controlled Trial	N = 77 Patients with CU N = 67 control			alfacalcidol administration and placebo			Chronic spontaneous urticaria	Serum 25(OH) D levels were significantly lower in CSU patients, negatively correlated with disease severity, and increased significantly after alfacalcidol treatment compared to placebo	*****

Table 1 (continued)

Author (References)	Year	Study design	No of participants	Age of participants	Gender (Male/female)	Vitamin D supplement vs control/plecabo	Baseline vitamin D status	Dose of vitamin D supplement	Types of chronic Urticaria	Clinical outcomes	Quality assessment
Nazila Ariaee et al. [10]	2017	Randomized controlled trial	N = 20	35.6 ± 13.1	9/11	Vitamin D supplement		50,000 unit every week	Chronic spontaneous urticaria	Vitamin D is a safe, cost-effective add-on to standard care for treating vitamin D-deficient chronic urticaria	******
Ilteris Oguz Topal et al. [11]	2016	Prospective Case control study	N = 58 CSU patients N = 45 controls			Vitamin D supplement		300 000 IU/month	Chronic spontaneous urticaria	Vitamin D replacement may improve symptom severity and quality of life in CSU patients	****
Qureshi SW et al. [12]	2025	Comparative cross-sectional study	N = 140		100% female	Vitamin D supplement was not administered		_	Chronic Urticaria	No association of UC with decreased serum level of vitamin D	****
Archana Mony et al.[13]	2020	Randomized Controlled Trial	N = 120 vitamin D-deficient CU patients Healthy control = N/A		25/95	vitamin D		60,000 IU per	Chronic Urticaria	Vitamin D supplementation reduces CU severity by lowering inflammation	***
Yu Ri Woo et al. [14]	2015	Retrospective case control Study	N = 72 diseased subjects N = 72 control	Chronic Urticaria = 37.89 ± 16.13, acute urticaria = 29.07 ± 17.07 atopic dermatitis = 21.83 ± 9.44 Healthy individuals = 38.61 ± 15.12	Chronic Urticaria = 28/44, acute urticaria = 12/44, atopic dermatitis = 13/13 Healthy individuals = 28/45	None	Lower vitamin D status	_	Chronic Urticaria, acute urticaria, atopic dermatitis	Serum vitamin D levels are often critically low in chronic urticaria patients	
Metin N et al. [15]	2021	Prospective Case control study	N = 60 subjects with chronic Urticaria N = 40 healthy individuals	18–65 years	Subjects = 19/41 Control = 14/26	None		_	Chronic Urticaria	Low vitamin D levels are significantly more frequent in CSU patients	

Table 1 (continued)

Author (References)	Year	Study design	No of participants	Age of participants	Gender (Male/female)	Vitamin D supplement vs control/plecabo	Baseline vitamin D status	Dose of vitamin D supplement	Types of chronic Urticaria	Clinical outcomes	Quality assessment
Masoud Movahedi et al. [16]	2015	Comparative cross-sectional study	N = 114 patients with chronic idiopathic urticaria N = 187 healthy volunteers as the control group						chronic idiopathic urticaria	Vitamin D levels positively correlate with urticaria activity, and deficiency may increase susceptibility to chronic idiopathic urticaria	

* represents the quality of study according to the Newcastle–Ottawa scale, one star means low quality, and seven stars represent best quality of evidence

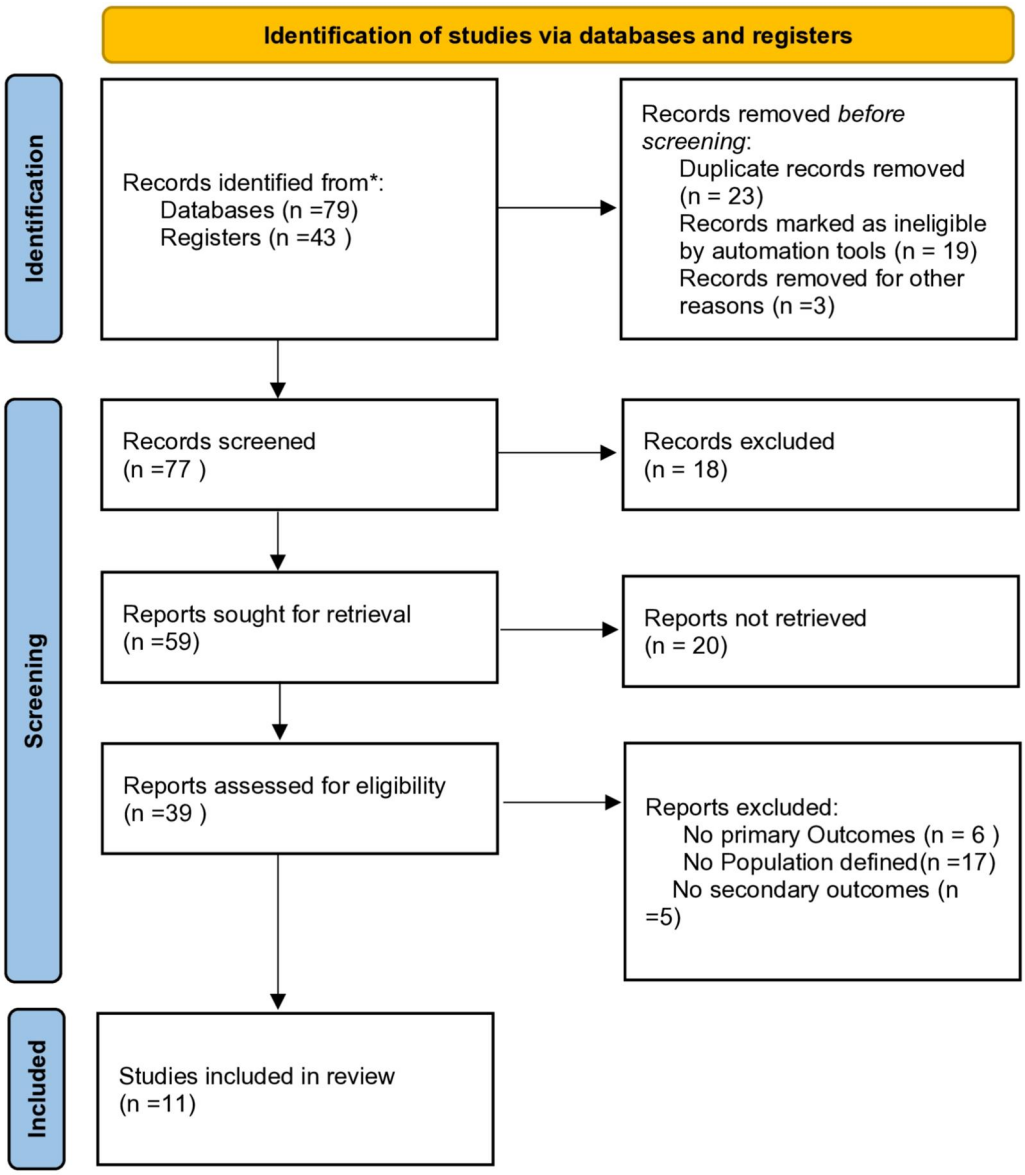

Fig. 1 Prisma flowchart

of participants, age and gender distribution, type and dose of vitamin D supplementation, baseline vitamin D levels, type of urticaria, and reported clinical outcomes. This process was carried out independently by two reviewers to minimize bias and ensure accuracy.

Risk of bias assessment

The risk of bias for randomized controlled trials was assessed using the Cochrane Risk of Bias Tool, evaluating domains such as randomization, blinding, and outcome reporting. For observational and case–control studies, the Newcastle–Ottawa Scale (NOS) was employed. Each study was rated as low, moderate, or high risk of bias based on these assessments. Disagreements were resolved through reviewer discussion.

Data synthesis

Due to heterogeneity in study design, vitamin D dosing, and outcome measures, a narrative synthesis approach was used to summarize findings. Key outcomes of interest included changes in urticaria activity score, symptom frequency and severity, and patient-reported quality of life following vitamin D supplementation.

Results

A total of 11 studies were included in this analysis, comprising 910 participants with chronic urticaria (CU) and 581 healthy controls (Table 1). These studies consisted of a mix of randomized controlled trials (RCTs), prospective and retrospective case–control studies, and cross-sectional analyses, conducted across various regions between 2014 and 2025.

Among the included studies, six studies investigated the therapeutic role of vitamin D supplementation in managing CU symptoms. These studies demonstrated a consistent trend showing that vitamin D, whether in the form of cholecalciferol (vitamin D_3), ergocalciferol (vitamin D_2), or alfacalcidol, improved clinical outcomes when used as an adjunct to standard therapy. For instance, Andy Rorie et al. (2014) reported that high-dose vitamin D_3 (4,000 IU/day) significantly enhanced symptom control in CU compared to a lower dose (600 IU/day). Similarly, Roohi Rasool et al. (2015) and Amal Ahmed Mohamed et al. (2022) found that vitamin D supplementation, when combined with antihistamines or corticosteroids, improved disease resolution and was associated with a significant rise in serum 25(OH)D levels. Nazila Ariaee et al. (2017) and Ilteris Oguz Topal et al. (2016) also confirmed the safety and clinical efficacy of high-dose vitamin D as an add-on therapy, contributing to symptom relief and better quality of life.

In contrast, five studies explored the association between vitamin D deficiency and CU without administering supplementation. These studies consistently reported that serum vitamin D levels were significantly lower in CU patients compared to healthy individuals. Tadech Boonpiyathad et al. (2014) found that lower 25(OH)D levels were significantly associated with chronic spontaneous urticaria (CSU), while Yu Ri Woo et al. (2015) and Masoud Movahedi et al. (2015) linked vitamin D deficiency with increased disease susceptibility and urticaria activity. Metin N et al. (2021) also observed a higher prevalence of deficiency in CSU patients. However, one outlier study by Qureshi SW et al. (2025), involving 140 female CU patients, reported no significant association between vitamin D status and the presence of urticaria, highlighting the need for further investigation.

Overall, the evidence from this review suggests a potential therapeutic benefit of vitamin D supplementation in patients with CU, particularly among those with documented deficiency. The majority of interventional studies indicated symptom improvement, reduced disease severity, and increased serum 25(OH)D levels following supplementation. Moreover, observational findings support the hypothesis that vitamin D plays an immunomodulatory role in CU pathogenesis. However, given the variability in study design, dosage, and baseline vitamin D levels, further large-scale, well-controlled RCTs are warranted to establish definitive clinical recommendations.

Discussion

The findings from this systematic review highlight a growing body of evidence supporting the potential role of vitamin D supplementation in the management of chronic urticaria (CU). Several included studies demonstrate that patients with CU often exhibit significantly lower serum levels of vitamin D compared to healthy controls, suggesting a possible association between vitamin D deficiency and the pathophysiology of the condition. While causality cannot be firmly established, the immunomodulatory properties of vitamin D provide a plausible mechanism by which supplementation may alleviate CU symptoms [17]. Vitamin D has been shown to inhibit the release of pro-inflammatory cytokines and modulate T-cell responses, both of which are relevant to the chronic inflammatory process underlying urticarial [18].

Clinical trials included in this review report varying outcomes regarding the efficacy of vitamin D supplementation in patients with CU. Some studies observed significant improvement in urticaria activity scores, reduced frequency and severity of wheals, and decreased use of antihistamines among patients receiving vitamin D, particularly in those who were deficient at baseline [6, 11, 13]. However, other studies showed minimal or no significant changes, suggesting that individual variability, dosage, baseline vitamin D levels, and duration of supplementation may influence outcomes [12]. These inconsistencies highlight the need for well-designed, large-scale randomized controlled trials to establish standardized protocols and to better define which patient populations are most likely to benefit [19].

This systematic review has several limitations that must be acknowledged. The included studies varied significantly in design, sample size, duration of intervention, and vitamin D dosage, which introduces heterogeneity and limits the ability to perform a quantitative meta-analysis. Many studies lacked rigorous randomization or blinding, increasing the risk of bias. Additionally, some trials did not account for confounding factors such as sun exposure, dietary intake, or baseline vitamin D status, which can influence serum levels and clinical outcomes. The majority of research also focused on short-term effects, with limited data on long-term safety and efficacy of supplementation in chronic urticaria patients.

Future perspectives

Future research should focus on conducting large-scale, randomized, double-blind, placebo-controlled trials to provide more definitive evidence on the role of vitamin

D in chronic urticaria. Studies should aim to standardize dosing protocols and clearly stratify participants based on baseline vitamin D levels to identify subgroups that may benefit most [20]. Furthermore, exploring the effects of vitamin D in different CU subtypes, such as autoimmune versus idiopathic urticaria, could yield insights into tailored treatment approaches. Longitudinal studies evaluating long-term outcomes and safety of vitamin D supplementation are also essential to determine its place in chronic urticaria management guidelines [21].

Conclusion

In conclusion, this systematic review highlights a consistent association between low serum vitamin D levels and chronic urticaria, particularly chronic spontaneous urticaria. The evidence suggests that vitamin D supplementation, especially in individuals with a deficiency, may serve as a safe, cost-effective, and beneficial adjunct therapy alongside standard treatments, leading to improvements in symptom severity, urticaria activity scores, and overall quality of life. Although a few studies reported no significant association, the majority support the potential role of vitamin D as an immunomodulatory agent in the management of chronic urticaria, warranting further high-quality trials to establish standardized dosing and long-term efficacy.

Author contributions

A.B. and C.D. wrote the main manuscript text and E.F. prepared Fig. 1. and G.H.I And J. K done the literature review and prepared the Table 1. All authors reviewed the manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Competing interests

The authors declare no competing interests.

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