Oftalmologi: Jurnal Kesehatan Mata Indonesia 2025, Volume 7, Number 3.
P-ISSN. 2723-6935, E-ISSN. 2541-4283
Received: 11 April 2025; Revised: 21 August 2025; Accepted: 28 August 2025

Vitamin D Levels in Adults with Allergic Conjunctivitis: A Systematic Review

Maria Evane Navy Cahaya Putri[1], Empi Irawan[1]
[1]RSPAL dr. Ramelan, Surabaya, Jawa Timur, Indonesia
**Correspondence: Maria Evane Navy Cahaya Putri, evanenavy@gmail.com*

How to Cite:
Putri, M. E. N. C., Irawan, E. (2025). Vitamin D Levels in Adults with Allergic Conjunctivitis: A Systematic Review. *Oftalmologi: Jurnal Kesehatan Mata Indonesia*, *7*(3), 95–99. https://doi.org/10.11594/ojkmi.v7i3.92

ABSTRACT
Introduction: Allergic conjunctivitis is an immune-mediated ocular inflammation, and this study reviews evidence on the association between vitamin D levels and disease severity in adults.
Methods: A systematic literature search was conducted using PubMed, Scopus, Web of Science, and Google Scholar for articles published between 2015 and 2025. Observational studies and clinical trials evaluating vitamin D status in adults with AC were included. Of 50 articles screened, four studies comprising 375 adult participants fulfilled the eligibility criteria. Extracted data included study design, vitamin D measurement methods, clinical outcomes, and statistical results. Risk of bias was assessed using ROBINS-I and Cochrane RoB 2.0, and the review followed PRISMA guidelines.
Results: The included studies consisted of two observational studies and two clinical trials. Lower vitamin D levels were significantly associated with more severe AC symptoms in two observational studies. One clinical trial demonstrated mild symptomatic improvement following vitamin D supplementation, while another showed no significant effect. Variations in diagnostic criteria, laboratory methods, and confounding factors limited comparability.
Conclusion: Lower vitamin D levels may enhance AC severity in adults. Further robust clinical trials are warranted to confirm these findings and to explore vitamin D supplementation's therapeutic role.
Keywords: Adults, Allergic Conjunctivitis, Immunomodulation, Systematic Review, Vitamin D

ABSTRAK
Pendahuluan: Konjungtivitis alergi (KA) merupakan kondisi inflamasi mata akibat hipersensitivitas. Vitamin D berperan dalam modulasi imun dan berpotensi memengaruhi penyakit alergi. Review ini bertujuan mensintesis bukti mengenai hubungan kadar vitamin D dengan keparahan KA pada dewasa.
Metode: Pencarian literatur dilakukan pada PubMed, Scopus, Web of Science, dan Google Scholar periode 2015–2025. Studi observasional dan uji klinis yang mengevaluasi status vitamin D pada pasien dewasa dengan KA dimasukkan. Dari 50 artikel yang disaring, 4 studi dengan total 375 subjek dewasa memenuhi kriteria inklusi. Data yang diambil meliputi desain studi, metode pengukuran vitamin D, hasil klinis, dan signifikansi statistik. Penilaian risiko bias menggunakan ROBINS-I dan Cochrane RoB 2.0. Proses review mengikuti pedoman PRISMA.
Hasil: Empat studi (dua observasional, dua uji klinis) memenuhi kriteria. Dua studi observasional melaporkan kadar vitamin D lebih rendah signifikan pada pasien KA berat (p=0,03 dan p=0,02). Satu uji klinis melaporkan perbaikan gejala ringan setelah suplementasi vitamin D (p=0,05), sementara satu lain tidak menunjukkan perbedaan bermakna (p=0,10). Perbedaan definisi diagnosis (konjungtivitis musiman vs. vernal), variasi metode pengukuran vitamin D (ELISA vs. HPLC), serta faktor pembaur yang tidak terkontrol (pola makan, paparan sinar matahari) membatasi perbandingan hasil antar studi.
Kesimpulan: Temuan mengindikasikan adanya hubungan antara kadar vitamin D rendah dan keparahan KA pada dewasa. Studi klinis lebih lanjut diperlukan untuk mengonfirmasi dan mengeksplorasi peran terapi suplementasi vitamin D.
Kata Kunci: Dewasa, Konjungtivitas Alergi, Modulasi Imun, Review Sistematis, Vitamin D

INTRODUCTION

Allergic conjunctivitis (AC) is characterized by ocular inflammation triggered by hypersensitive reactions to environmental allergens. Manifestations include itching, redness, tearing, and photophobia. Globally, AC is estimated to affect up to 15–40% of the population, with higher prevalence in urban and industrialized areas, while studies in Asia—including Indonesia—have reported prevalence rates ranging from 10–20% among outpatients with ocular complaints. The pathogenesis involves IgE-mediated mast cell activation, releasing histamine and other inflammatory agents. [1,2]

The fat-soluble hormone vitamin D modulates the immune system. It works by interacting to the vitamin D receptor (VDR) on T, B, and dendritic cells.[3,4] Vitamin D helps maintain immune equilibrium by suppressing Th2 responses and enhancing regulatory T cell development. Moreover, it induces antimicrobial peptides that contribute to immune defense.[5,6]

Globally, vitamin D deficiency is a recognized public health issue with implications for immune dysregulation and allergic diseases.[7,8] Supplementation has shown efficacy in managing allergic conditions including asthma and atopic dermatitis.[9,10]

Although data links vitamin D deficiency with several allergic diseases, AC studies are few and inconsistent. Some say vitamin D levels inversely affect AC severity; others find no significant correlation, likely due to population and methodological differences.[11,12] Additionally, current vitamin D intake guidelines may not fully address immunomodulatory needs.[7,8] The objective of this review is to synthesize and critically evaluate current evidence on the association between vitamin D levels and allergic conjunctivitis severity in adult populations, with the aim of clarifying its potential as a therapeutic target in AC management.

METHODS

A systematic search was undertaken in PubMed, Scopus, Web of Science, and Google Scholar 2015–2025 articles. Keywords included 'Vitamin D,' 'Allergic Conjunctivitis,' 'Adults,' 'Observational Studies,' and 'Clinical Trials.' The search strategy was developed with a research librarian to maximize retrieval.

Included studies were observational or clinical trials measuring vitamin D levels in adults with AC diagnosis. Excluded were pediatric studies, case reports, articles without clear diagnostic criteria, and non-English publications. Studies without specific AC diagnosis were also excluded.

Two reviewers independently extracted data using a Cochrane Handbook-adapted form. Extracted data covered study design, sample size, diagnostic methods, vitamin D assay types (e.g., ELISA, HPLC), statistical outcomes, clinical findings, and confounding variables (diet, sun exposure). Disagreements were resolved by consensus.

Data accuracy was verified against original publications. Authors were contacted for missing data when needed.

Bias risk was evaluated using ROBINS-I for observational studies and Cochrane RoB 2.0 for clinical trials, covering confounding, selection, measurement, and reporting biases. Discrepancies were resolved through discussion.

The review followed PRISMA guidelines to enhance transparency and reproducibility.

Due to heterogeneity in methods and outcomes, results were synthesized narratively. Meta-analysis was not conducted.

Screening results were: 50 records identified; 50 screened; 15 full texts assessed; 10 excluded; 4 studies included.

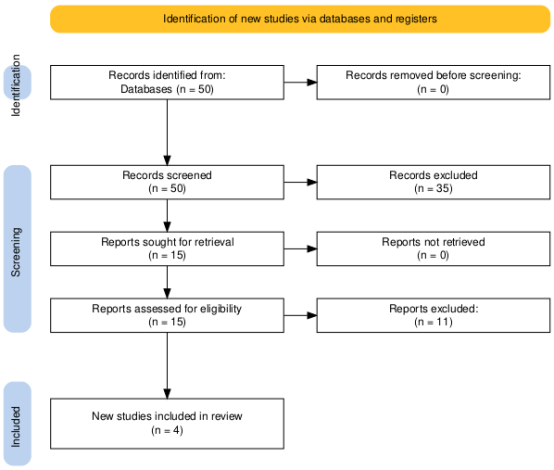

Figure 1. Flowchart depicting the process of study selection for the systematic review on vitamin D status in adult patients with allergic conjunctivitis

RESULTS

Four studies met the inclusion criteria, encompassing two observational studies and two clinical trials, all focusing on adult patients diagnosed with allergic conjunctivitis. Due to variability in study designs, diagnostic approaches, and methods for measuring vitamin D levels, direct comparisons were limited. Key characteristics of these studies, including sample sizes, diagnostic criteria, vitamin D levels, and statistical significance, are summarized in Table 1. An evaluation of the risk of bias for each study, based on established assessment tools, is presented in Table 2.

Table 1. Summary of study designs and key characteristics of included research on vitamin D levels in adults with allergic conjunctivitis

Study	Authors	Year	Study Design	Sample Size	Diagnostic Criteria	Vitamin D Level (ng/mL)	p-value	Key Findings
Study 1	Dadaci et al.	2014	Observational	100	Seasonal AC confirmed by IgE (Adults)	18.5 ± 5.2	0.03	Lower vitamin D correlated with increased symptom severity[13]
Study 2	Yenigun et al.	2015	Clinical Trial	75	Allergic rhinoconjunctivitis, positive skin prick test	21.0 ± 6.3	0.10	No significant difference in vitamin D between groups[11]
Study 3	Sorkhabi et al.	2020	Observational	120	Vernal keratoconjunctivitis clinically diagnosed	16.8 ± 4.9	0.02	Significantly lower vitamin D in severe AC cases[12]
Study 4	Al-Wailmi et al.	2021	Clinical Trial	80	Seasonal AC confirmed by IgE (Adults)	23.5 ± 7.1	0.05	Mild symptom improvement with vitamin D supplementation[14]

DISCUSSION

This review suggests vitamin D deficiency may worsen allergic conjunctivitis in adults. Observational studies by Dadaci et al. and Sorkhabi et al. found significantly lower vitamin D levels in severe AC cases, suggesting vitamin D insufficiency may worsen ocular inflammation via Th2 pathways.[1,2]

Yenigun et al.'s clinical trial showed no significant vitamin D differences between groups, possibly due to population and diagnostic heterogeneity. Conversely, Al-Wailmi et al. demonstrated mild symptomatic benefits following vitamin D supplementation, supporting therapeutic potential. These findings align with mechanistic studies highlighting vitamin D's immunomodulatory effects, including Treg promotion and Th2 suppression.[3,4]

Variability in vitamin D assays (ELISA vs. HPLC) and incomplete control for confounders like sun exposure and diet limit study comparability.[15] Residual confounding remains a concern, particularly in cross-sectional studies.

While mild symptom improvement post-supplementation is promising, optimal dosing and duration for AC remain undefined. Similar benefits in asthma and atopic dermatitis have been observed with daily vitamin D doses of 1000–2000 IU.[9,10]

Overall, the current evidence base is limited by heterogeneity in study designs, small sample sizes, and methodological inconsistencies. Future research should prioritize well-designed, adequately powered clinical trials that control for potential confounders and utilize standardized vitamin D assays. Furthermore, exploring the effects of vitamin D supplementation on specific inflammatory markers such as IL-4, IL-10, and TGF-β may provide valuable mechanistic insights and inform clinical practice. Moving forward, collaborative multicenter trials with long-term follow-up are essential to establish causality, define optimal supplementation strategies, and ultimately translate these findings into clear clinical guidelines for the management of allergic conjunctivitis.[2]

Table 2. Evaluation of methodological bias in included studies using ROBINS-I and Cochrane RoB 2.0 frameworks

Study	Bias Domain	Study Design	Bias Judgment	Justification
Dadaci et al. (2014)	Confounding	Observational	Moderate	Potential confounding due to unmeasured seasonal and dietary factors
	Selection Bias		Low	Clear IgE-based diagnostic criteria
	Measurement Bias		Low	Valid ELISA vitamin D assays
	Reporting Bias		Moderate	Incomplete subgroup analysis reporting
Yenigun et al. (2015)	Randomization Process	Clinical Trial	Low	Computer-generated randomization
	Deviations from Intended Intervention		Moderate	Unclear participant blinding
	Reporting Bias		High	Selective reporting suggested by incomplete p-value data
Sorkhabi et al. (2020)	Confounding	Observational	Low	Adjusted for age, gender, BMI, symptom duration
	Measurement Bias		Low	Sensitive HPLC vitamin D measurement
	Reporting Bias		Low	Complete outcome reporting
Al-Wailmi et al. (2021)	Randomization Process	Clinical Trial	Low	Block randomization method
	Reporting Bias		Low	Outcomes reported per protocol

CONCLUSION

Lower vitamin D levels could worsen allergic conjunctivitis in adults. Although observational data supports this, clinical trials remain inconclusive due to methodological differences. Mild benefits from vitamin D supplementation warrant further research. Clinicians should consider vitamin D status evaluation in patients with recurrent or severe AC. High-quality trials are needed to establish supplementation protocols and clarify immunological mechanisms.

REFERENCE

1. Zhang P, Xu Q, Zhu R. Vitamin D and Allergic Diseases. Vol. 15, Frontiers in Immunology. Frontiers Media SA; 2024.
2. Szydziak J, Hrapkowicz A, Janowska K, Dąbkowska D, Szeidl O, Rehan D, et al. The Role of Vitamin D in Allergic Diseases. Quality in Sport. 2024 Nov 12;31.
3. Lee HS, Kwon JY, Rho CR, Mok J, Joo CK. Vitamin D Supplementation Modulates Th2 Immune Response by Inducing T Regulatory Cells in Allergic Conjunctivitis. Invest Ophthalmol Vis Sci. 2017 Jun;58(8).
4. Johnson CR, Thacher TD. Vitamin D: Immune Function, Inflammation, Infections and Auto-immunity. Paediatr Int Child Health. 2023 Mar;43:29–39.
5. Wang TT, Nestel FP, Bourdeau V, Nagai Y, Wang Q, Liao J, et al. Cutting Edge: 1,25-Dihydroxyvitamin D3 Is a Direct Inducer of Antimicrobial Peptide Gene Expression. The Journal of Immunology. 2004 Sep 1;173(5):2909–12.
6. Lathers CM, Rapp D. Immunomodulatory Roles of Vitamin D: Implications for Autoimmune Diseases. Autoimmune Reviews. 2010;9(8):637–44.
7. Holick MF. Vitamin D Deficiency. N Engl J Med [Internet]. 2007 Jul 19;357:266–81. Available from: www.nejm.org
8. Heaney RP, Holick MF. Why the IOM Recommendations for Vitamin D are Deficient. The Journal of Bone and Mineral Research. 2011 Mar;26(3):455–7.
9. Camargo CA, Ganmaa D, Ginde AA, Sidbury R. Vitamin D in Atopic Dermatitis, Asthma and Allergic Diseases. Annals of Allergy, Asthma & Immunology. 2014;113(5):409–15.
10. Martineau AR, Jolliffe DA, Hooper RL, Greenberg L, Aloia JF, Bergman P, et al. Vitamin D Supplementation to Prevent Acute Respiratory Tract Infections: Systematic Review and Meta-Analysis of Individual Participant Data. BMJ. 2017 Feb 15;356.
11. Yenigun A, Dadaci Z, Oncel M. Plasma Vitamin D Levels of Patients with Allergic Rhinoconjunctivitis with Positive Skin Prick Test. Am J Rhinol Allergy. 2015 Mar 1;29(2):46–9.
12. Sorkhabi R, Ahoor MH, Ghorbanihaghjo A, Jafari S. Serum Vitamin D Levels in Patients with Vernal Keratoconjunctivitis and Its Relationship with Disease Severity. Eur J Ophthalmol. 2020 Nov 14;31(6):1–6.
13. Dadaci Z, Borazan M, Kiyici A, Oncel Acir N. Plasma Vitamin D and Serum Total Immunoglobulin E Levels in Patients with Seasonal Allergic conjunctivitis. Acta Ophthalmol. 2014 Feb 16;92(6):443–6.
14. Al-Swailmi FK, Shah SIA, Al-Mazaideh GM, Sikandar MZ. Serum Vitamin D and Immunoglobulin E Levels In Patients With Seasonal Allergic Conjunctivitis. IIUM Medical Journal Malaysia [Internet]. 2021 Jul;20(3):79–83. Available from: https://journals.iium.edu.my/kom/index.php/imjm/article/view/1756
15. Chan HN, Zhang XJ, Ling XT, Bui CHT, Wang YM, Ip P, et al. Vitamin D and Ocular Diseases: A Systematic Review. Vol. 23, International Journal of Molecular Sciences. MDPI; 2022.