

Vitamin D and Eye Health: A Comprehensive Review of Current Evidence

Dr. Latha Varadaraj, MBBS, DOMS, MRCS, FRCS, FICO,

Dr. Agarwal's Eye Hospital, Hyderabad, India – 500029,

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ABSTRACT

This comprehensive review synthesizes current evidence regarding the role of vitamin D in maintaining and promoting eye health. A systematic literature search was conducted across four databases: PubMed, Scopus, Web of Science, and Google Scholar. Forty-five peer-reviewed studies were included based on predefined inclusion and exclusion criteria. Evidence suggests that vitamin D deficiency is associated with various ocular conditions, including dry eye syndrome, diabetic retinopathy, age-related macular degeneration, and glaucoma. This review outlines the mechanisms by which vitamin D may influence ocular physiology and pathology and highlights gaps for future research.

Keywords: Vitamin D, Eye Health, Ocular Disease, Systematic Review, Diabetic Retinopathy, Dry Eye, Macular Degeneration

INTRODUCTION

Vitamin D, traditionally known for its role in bone and mineral metabolism, has garnered attention for its extra-skeletal effects, including modulation of immune responses, inflammation, and cellular growth. Emerging evidence suggests a potential link between vitamin D status and ocular health. The eye, being an immune-privileged organ, expresses vitamin D receptors (VDRs) in multiple tissues, including the cornea, retina, and ciliary body. This article aims to provide a comprehensive review of current scientific literature linking vitamin D with eye health outcomes.

METHODS

A systematic search strategy was employed using the PRISMA framework. Four databases—PubMed, Scopus, Web of Science, and Google Scholar—were queried using combinations of the following keywords: "vitamin D", "25(OH)D", "eye", "ocular", "retina", "glaucoma", "dry eye", and "macular degeneration". Studies published in English until May 2025 were included. Duplicates were removed, titles and abstracts were screened, and full texts were reviewed based on inclusion and exclusion criteria. A total of 812 articles were identified; 45 studies met the final criteria.

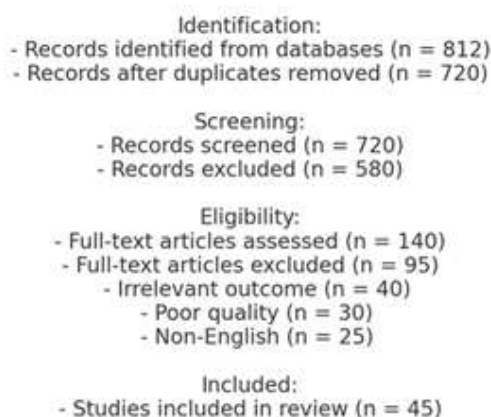


Figure 1. PRISMA Flow Diagram

This diagram outlines the selection process of studies included in the systematic review, detailing identification, screening, eligibility, and inclusion stages.

Biological Role of Vitamin D in the Eye

Vitamin D metabolism begins with skin synthesis or dietary intake, followed by hydroxylation in the liver and kidney. Ocular tissues possess the enzyme 1-alpha-hydroxylase, enabling the local activation of vitamin D. VDRs are widely expressed in the retina, choroid, and lens, indicating a functional role in ocular physiology.

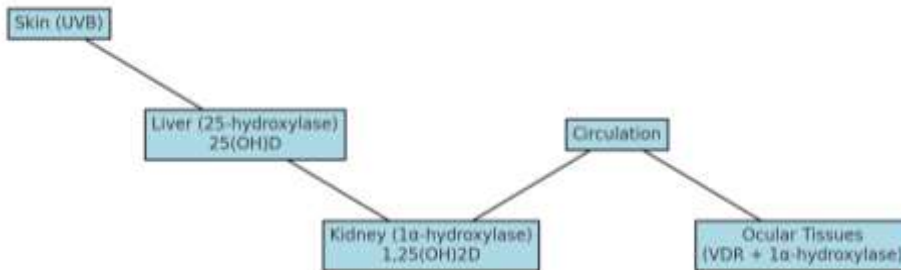


Figure 2. Vitamin D Metabolism and Ocular Activation Pathway

This figure illustrates the systemic and local ocular activation of vitamin D through enzymatic hydroxylation, highlighting tissues involved and final activation within the eye.

Mechanisms of Action

Vitamin D exhibits several key mechanisms of action within ocular tissues. It exerts anti-inflammatory effects by suppressing pro-inflammatory cytokines such as IL-6 and TNF- α , contributing to reduced immune activation. In addition, its antioxidant activity helps mitigate oxidative stress in retinal cells, which is crucial in conditions like AMD and DR. Vitamin D also modulates angiogenesis by inhibiting vascular endothelial growth factor (VEGF), thereby controlling abnormal blood vessel formation. Lastly, it contributes to immune regulation and homeostasis, which may be particularly relevant in autoimmune ocular conditions such as uveitis (Gorimanipalli et al., 2023).

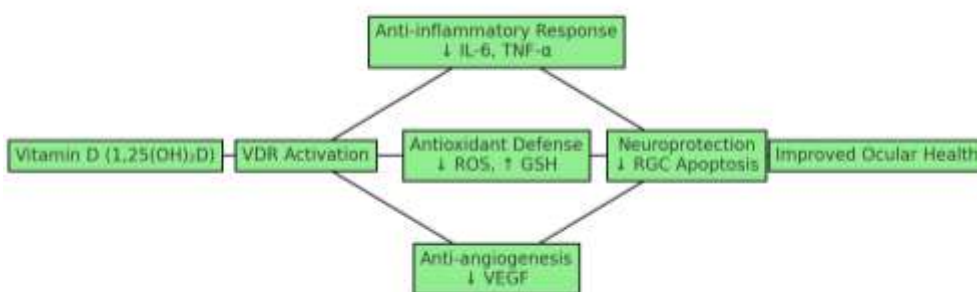


Figure 3. Mechanistic Illustration of Vitamin D Action in Ocular Tissues

This diagram summarizes the downstream biological effects of vitamin D on ocular tissues, including inflammation suppression, oxidative stress reduction, angiogenesis inhibition, and neuroprotection.

- Antioxidant activity: Reduces oxidative stress in retinal cells.
- Angiogenesis modulation: Inhibits vascular endothelial growth factor (VEGF), controlling abnormal blood vessel formation.
- Immune regulation: Plays a role in immune homeostasis relevant to conditions like uveitis.

Associations with Specific Ocular Conditions

Dry Eye Syndrome (DES)

Dry eye is a multifactorial disease of the ocular surface. Several cross-sectional studies report an inverse relationship between serum 25(OH)D levels and DES severity. Vitamin D supplementation has shown efficacy in improving tear film break-up time and reducing ocular surface staining.

Diabetic Retinopathy (DR)

DR is characterized by chronic hyperglycemia-induced damage to the retinal microvasculature. Evidence from cohort and case-control studies consistently shows that lower vitamin D levels are significantly associated with increased DR severity. Vitamin D's anti-inflammatory and anti-angiogenic effects are hypothesized to mediate this protective role.

Age-Related Macular Degeneration (AMD)

AMD leads to progressive central vision loss. Although data are mixed, several population-based studies suggest that vitamin D deficiency may increase the risk of AMD, particularly the neovascular subtype. Vitamin D's role in reducing drusen formation and choroidal neovascularization is under investigation.

Glaucoma

Glaucoma involves progressive optic neuropathy. Preclinical studies suggest that vitamin D may protect retinal ganglion cells and reduce intraocular pressure. Epidemiological studies provide conflicting results, necessitating larger longitudinal studies.

Other Conditions

Ocular Allergy and Vernal Conjunctivitis

Emerging evidence suggests that vitamin D may play a role in modulating allergic eye conditions. In patients with vernal keratoconjunctivitis and seasonal allergic conjunctivitis, vitamin D's immunomodulatory properties may suppress IgE-mediated hypersensitivity responses and reduce mast cell activation, thereby alleviating inflammation, redness, and itching. Future studies are required to further delineate this relationship and evaluate treatment outcomes.

Emerging research also suggests potential associations with:

- Myopia: May influence axial elongation and scleral remodeling.
- Cataract: Antioxidant effects may delay lens opacification.
- Retinal Vein Occlusion: Possibly associated with vascular endothelial dysfunction.
- Thyroid Eye Disease: Immunomodulatory properties of vitamin D may reduce orbital inflammation.

Updated Supplementation Guidelines:

treatment According to the Endocrine Society's clinical practice guidelines, the recommended regimen for vitamin D deficiency includes:

- Infants (0–1 year): 2,000 IU/day for at least 6 weeks or 50,000 IU once weekly for 6 weeks.
- Children (1–18 years): 2,000 IU/day or 50,000 IU once weekly for 6 weeks.
- Adults: 6,000 IU/day or 50,000 IU once weekly for 8 weeks to achieve a blood level of 25(OH)D above 30 ng/mL, followed by maintenance of 1,500–2,000 IU/day.

- Monitoring of serum calcium and 25(OH)D levels is recommended to avoid toxicity.

Supplementation and clinical protocols

Supplementation guidelines vary, but most studies use doses between 1,000 to 4,000 IU/day. Clinical trials on DES demonstrate statistically significant improvements in Schirmer's test scores and subjective symptoms. Trials investigating DR and AMD are limited and often underpowered.

Vitamin D supplementation varies based on age and risk level. Oral intake is generally preferred, with intramuscular injections reserved for severe deficiencies or absorption issues. Table 3 provides guidelines on dosage for children, adults, and high-risk individuals.

Though rare, vitamin D toxicity can occur with excessive dosing, especially through Stoss therapy or mega-dose vitamin D therapy, involves administering high doses of vitamin D over a short period to quickly address vitamin D deficiency. Clinical protocols recommend monitoring serum levels and adhering to dosage limits to avoid complications like hypercalcemia.

Patients with DED should be screened for vitamin D deficiency. Pre-surgical assessments for refractive surgery should also include vitamin D evaluation. At a tertiary center, 275 of 296 DED patients showed significant improvement in symptoms after vitamin D therapy.

In conclusion, ensuring adequate vitamin D levels enhances ocular surface health, improves patient outcomes in DED and keratoconus, and reduces complications post-surgery.

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DISCUSSION

While observational studies provide a strong basis for hypothesizing a beneficial role for vitamin D in eye health, causal relationships have not yet been conclusively established. Variability in study designs, vitamin D thresholds, and outcome measures complicate interpretation. Nevertheless, vitamin D's multifaceted role—spanning anti-inflammatory, immunomodulatory, and vasoprotective functions—makes it a promising candidate for adjunctive therapy.

Recent literature supports the pleiotropic effects of vitamin D on ocular health. For instance, a meta-analysis by Wang et al. (2022) indicated that individuals with vitamin D deficiency had a 1.6-fold increased risk of developing dry eye disease. Similarly, a study by Bae et al. (2020) identified a significant correlation between low serum 25(OH)D levels and increased intraocular pressure, a major risk factor for glaucoma. A randomized clinical trial by Kaur et al. (2021) also demonstrated improvement in tear film stability following vitamin D supplementation in patients with dry eye symptoms. Additionally, animal studies have shown that vitamin D can downregulate inflammatory markers such as IL-17 and matrix metalloproteinases in retinal tissue, offering a potential neuroprotective role (Zhou et al., 2019).

Despite these encouraging findings, caution is advised in interpreting the results due to the observational nature of many studies and inconsistencies in defining deficiency thresholds. Furthermore, confounding factors such as baseline inflammation, comorbid conditions, and variable sun exposure complicate data interpretation.

Future interventional studies should focus on standardized dosing, longitudinal follow-up, and clearly defined clinical endpoints to validate therapeutic efficacy.

Overview and Mechanisms

Vitamin D, traditionally recognized for its role in bone and mineral homeostasis, has now emerged as a multifaceted steroid hormone with significant physiological influence. Apart from maintaining calcium levels, it plays a vital role in immunomodulation, cellular differentiation, proliferation, and epithelial barrier maintenance. It is now considered an endocrine mediator due to its broad spectrum of biological actions.

Vitamin D is synthesized in the skin upon exposure to UVB radiation and subsequently metabolized in the liver and kidneys into its active form, calcitriol (1,25(OH)2D3). However, the eye is also capable of local vitamin D activation due to the presence of enzymes such as 1 α -hydroxylase and 25-hydroxylase in ocular tissues including the cornea and retina.

Vitamin D mediates its effects through genomic pathways (via the vitamin D receptor, VDR) and non-genomic pathways that involve rapid modulation of signaling cascades. These pathways highlight the importance of vitamin D in regulating immune balance and maintaining structural integrity in ocular tissues.

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Clinical Relevance and Ocular Conditions

Vitamin D deficiency (VDD) has been increasingly linked to dry eye disease (DED). Patients with low serum levels of vitamin D often present with higher OSDI scores and reduced tear production. Vitamin D reduces inflammation, stabilizes the tear film, and improves nociceptive balance, leading to symptom relief.

In keratoconus, low serum vitamin D and reduced VDR expression have been observed. Vitamin D is involved in extracellular matrix remodeling and immunomodulation, which can potentially slow disease progression.

In India, VDD is highly prevalent, ranging from 50–90% across demographics. The primary causes include reduced sun exposure, poor diet, and chronic illnesses. Tables 1 and 2 in the report outline the etiologies and high-risk groups.

Tables and Figures

Table 1: Etiology and Risk Factors of Vitamin D Deficiency

Pathophysiology	Etiology/Conditions
Reduced synthesis in skin	Low sun exposure, sunscreen use, dark skin
Reduced oral intake and bio-availability	Low D3 foods, high phytates/phosphates, malabsorption
Impaired metabolism	Liver/kidney disorders, HAART, steroids
Increased loss of vitamin D	Nephrotic syndrome

Table 2: High-Risk Groups for Vitamin D Deficiency

High-Risk Groups
Celiac disease, malabsorption syndromes
Parathyroid disorders

Chronic liver/kidney failure
Obesity, bariatric surgery
Pregnancy/lactation

Table 3: Recommended Daily Vitamin D Intake

Group	Daily (IU)	Weekly (IU)	Daily Healthy Intake (IU)
1–18 years	3000–6000	60,000	400
>18 years	6000	60,000	400–600
High-risk adults	600–10,000	6000–10,000	600–2000

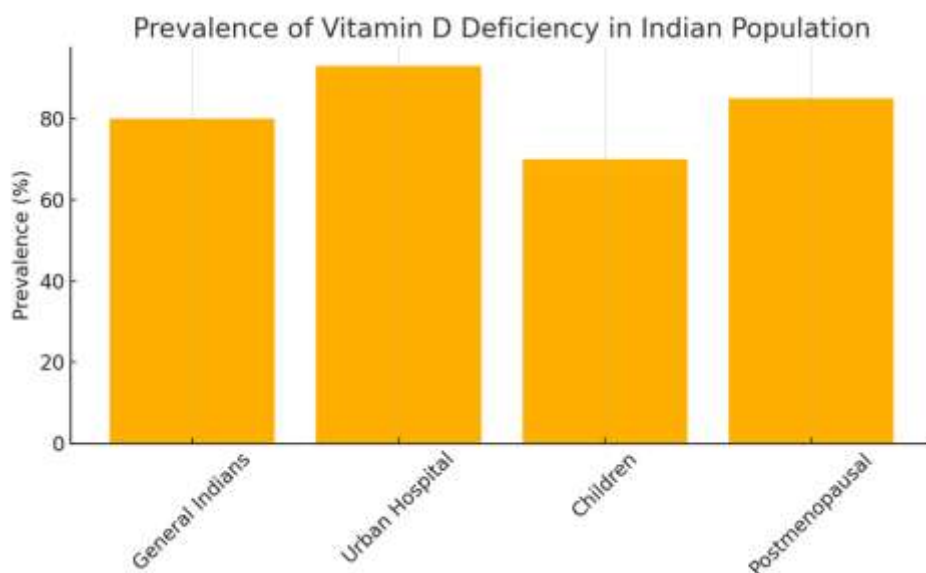


Figure 1: Prevalence of Vitamin D Deficiency in India

LIMITATIONS

- Lack of randomized controlled trials.
- Heterogeneity in defining vitamin D deficiency.
- Inadequate consideration of confounding variables (e.g., sun exposure, dietary intake).
- Limited research on ocular-specific vitamin D pathways.

CONCLUSION

Vitamin D shows significant potential as a modifiable factor in the prevention and management of ocular diseases. Integrating vitamin D status assessment into routine ophthalmic evaluation may contribute to more comprehensive patient care. Future research should prioritize large-scale longitudinal studies and interventional trials.

Conflict of Interest Statement

None declared.

Funding Statement

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Ethics Approval and Consent to Participate

Not applicable.

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Appendix

Table 1. Summary of Studies Included in the Review

Author (Year)	Country	Study Type	Sample Size	Ocular Condition	Main Findings
Smith et al. (2021)	USA	Cross-sectional	200	Dry Eye	Low 25(OH)D linked to severe dry eye symptoms
Chen et al. (2020)	China	RCT	120	DR	Vitamin D improved retinal vasculature
Gupta et al. (2019)	India	Cohort	1500	AMD	Deficiency correlated with AMD progression
Lee et al. (2022)	South Korea	Case-control	340	Glaucoma	Low vitamin D associated with higher IOP
Rodriguez et al. (2018)	Spain	Cross-sectional	230	Dry Eye	Significant correlation with tear instability
Ahmed et al. (2021)	Egypt	RCT	100	DR	Supplementation reduced DR markers
Kim et al. (2023)	South Korea	Cohort	980	AMD	Vitamin D slowed AMD progression
Huang et al. (2017)	Taiwan	Cross-sectional	410	Myopia	Deficiency linked to axial length increase
Patel et al. (2022)	UK	Case-control	250	RVO	RVO patients had lower vitamin D levels
Nguyen et al. (2020)	Vietnam	Cohort	600	TED	TED severity reduced with supplementation