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Vitamin D and Glaucoma Risk: Current Evidence and Therapeutic Implications

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Abstract

Introduction and purpose

Glaucoma is a chronic, progressive optic neuropathy and a leading cause of irreversible blindness worldwide. Increasing evidence suggests that, beyond intraocular pressure, systemic and metabolic factors may contribute to its pathogenesis. Vitamin D, known for its immunomodulatory and neuroprotective properties, has emerged as a potential factor influencing glaucoma risk. The aim of this study was to evaluate the relationship between vitamin D supplementation and the risk of developing glaucoma.

Material and method

A narrative review of current literature, including experimental, observational, and clinical studies, was conducted to assess the association between vitamin D status, supplementation, and glaucoma-related outcomes such as intraocular pressure and optic nerve damage. Particular attention was given to studies analyzing serum 25(OH)D levels, supplementation patterns, and disease progression.

Results

Experimental studies indicate that calcitriol may reduce intraocular pressure and improve aqueous humor outflow, while observational studies often demonstrate an inverse relationship between serum vitamin D levels and glaucoma risk. However, clinical trials assessing supplementation have yielded inconclusive results, with some showing no significant effect on intraocular pressure. Variability in study design, population characteristics, and lack of detailed supplementation data limit the interpretation of findings. Additionally, vitamin D may exert neuroprotective effects independent of pressure regulation.

Conclusions

Vitamin D may play a supportive role in glaucoma prevention through systemic and ocular mechanisms however, current evidence is insufficient to confirm a clear protective effect of supplementation. Further large-scale, well-designed prospective studies are required to clarify its clinical significance.

Keywords: Glaucoma; Vitamin D; Intraocular pressure (IOP); Neuroprotection; Calcitriol; Optic nerve damage

1. Background

Glaucoma is a chronic progressive optic neuropathy that is recognized as a leading cause of irreversible blindness globally, with an estimated 76 million individuals affected in 2020, a number expected to rise to 111.8 million by 2040 [1] [2]. Traditional understanding of glaucoma focuses on intraocular pressure and optic nerve damage. One of the main risk factors is high intraocular pressure (IOP), which is usually brought on by increased resistance to fluid drainage through the trabecular meshwork. Retinal ganglion cells are specifically lost as a result of the illness. The weakening of the macular ganglion cell complex (GCC) and ultimately the retinal nerve fiber layer (RNFL) frequently precedes this [9]. Additionally, recent studies have connected oxidative stress, persistent neuroinflammation, and mitochondrial dysfunction to the advancement of illness [10]. However, emerging evidence suggests that systemic factors, including vascular, metabolic, and inflammatory pathways, may significantly contribute to the disease's development and progression [7] [5].

The disease predominantly impacts older adults, many of whom have concurrent chronic conditions such as hypertension, diabetes, and chronic kidney disease. These results suggest that glaucoma may be a clinical sign of a more widespread systemic susceptibility, suggesting that people with glaucoma require holistic health care [7].

The main sign of developing glaucoma is visual field loss, which is one of the symptoms and consequences. It can be classified as early, moderate, or advanced based on the degree of visual field loss [9]. If left unmanaged, the damage to the optic nerve becomes permanent and leads to gradual vision loss [10] as well as irreversible blindness. [9] While some forms of glaucoma (like angle-closure) can cause acute symptoms, the sources primarily focus on the asymptomatic and progressive nature of open-angle glaucoma, emphasizing that it often goes unnoticed until significant damage has occurred [9].

1.1. Types of Glaucoma: Key Categories and Subtypes

Glaucoma is not a single disease but a group of conditions that damage the optic nerve and can cause irreversible vision loss. Research divides glaucoma mainly by how the eye's drainage angle looks, the cause (primary vs secondary), and age of onset.

Major Adult Categories

By drainage angle anatomy

- **Open-angle glaucomas**: Drainage angle looks open; outflow is impaired.
  Includes:
  - Primary open-angle glaucoma (POAG) – the most common type worldwide and in many series [20,21,22,23]
  - Normal-tension glaucoma (NTG) – optic nerve damage with IOP in the normal range; considered an open-angle subtype [24,25,26,27]
  - Juvenile open-angle glaucoma (JOAG) – early-onset open-angle disease in young people [25,28,29]
  - Ocular hypertension – high pressure with no established damage; often grouped with open-angle conditions [25,26].
- **Angle-closure glaucomas**: Iris blocks the drainage angle.
  - Primary angle-closure disease (spectrum including suspects, acute, intermittent, chronic angle-closure) [25, 21, 30, 27]
  - Acute and chronic forms are often separated (AACG vs CACG) [26,27]

Childhood / Pediatric Glaucoma

Childhood glaucoma is classified separately by the Childhood Glaucoma Research Network (CGRN) [33,28,29,34]:

- Primary:
  - Primary congenital glaucoma (PCG) – from birth or early infancy [33,28,29,30]
  - Juvenile open-angle glaucoma.
- Secondary:
  - Following cataract surgery.
  - Associated with nonacquired ocular anomalies (e.g., Axenfeld-Rieger, Peters anomaly, aniridia).
  - Associated with nonacquired systemic syndromes (e.g., Sturge-Weber, neurofibromatosis).
  - Associated with acquired conditions (uveitis, trauma, tumors) [28,29,34].
- **Selected Named Secondary Types**
  - Neovascular glaucoma – due to new abnormal blood vessels; highlighted as a key secondary, often severe type [25,26,31,32].

- Lens-related / phacogenic glaucomas – lens-induced, phacomorphic, phacolytic, etc., grouped as phacogenic secondary glaucomas [31,32]
- Other secondary open-angle forms include pigmentary, pseudoexfoliation, steroid-induced, and glaucomas associated with inflammation, trauma, aphakia/pseudophakia, and retinal disorders [21,22,25,26]

1.2. Pharmacokinetics and Pharmacodynamics of Vitamin D.

Vitamin D plays a crucial role in maintaining systemic health, with functions extending beyond calcium homeostasis to include immune modulation, cellular differentiation, and neuroprotection [3] [4]. Vitamin D is a class of fat-soluble prohormones consisting of vitamin D2 and vitamin D3 (cholecalciferol) (Figure 1). Vitamin D can be directly absorbed from the diet as vitamin D3 and vitamin D2 (ergocalciferol) or created in the skin from 7-

dehydrocholesterol under the influence of UV radiation, known as vitamin D3 (cholecalciferol) [17]. The liver's cytochrome P450 (CYP)2R1 and 27A1 then hydroxylate either form to 25-hydroxycholecalciferol (calcidiol or calcifediol, 25(OH)D).The active form of vitamin D3, 1α,25-dihydroxyvitamin D (1,25(OH)2D or calcitriol), is then produced mostly in the kidney by 25-hydroxyvitamin D3-1α-hydroxylase (CYP27B1). Extrarenal tissues include the skin, brain, pancreas, colon, breast, ovary, muscle, immune cells/macrophages, and nonparenchymal hepatic cells express CYP27B1 to a lesser extent [18]. Consequently, it is difficult for these tissues to produce 1,25(OH)2D locally [19]. 24-hydroxylase (CYP24A1) transforms excess active vitamin D (1,25(OH)2D) into inactive metabolites (1,24,25(OH)3D). 1,25(OH)2D induces CYP24A1 through a feed-forward mechanism. CYP27B1 inhibits the formation of 1,25(OH)2D, which is the feedback mechanism.

Additionally, 25(OH)D is converted by CYP24A1 to another inactive metabolite, 24,25-dihydroxyvitamin D3, which is another way to prevent excessive quantities of moderate or highly active vitamin D metabolites from circulating. Vitamin D shortage can result from disproportionate delivery of the hormonal form of vitamin D (1,25(OH)2D), which stimulates the breakdown of 25(OH)D. This is significant since 24,25-dihydroxyvitamin D2 shows 100% cross-reactivity with the majority of assays used to assess circulating 25(OH)D to estimate vitamin D status.

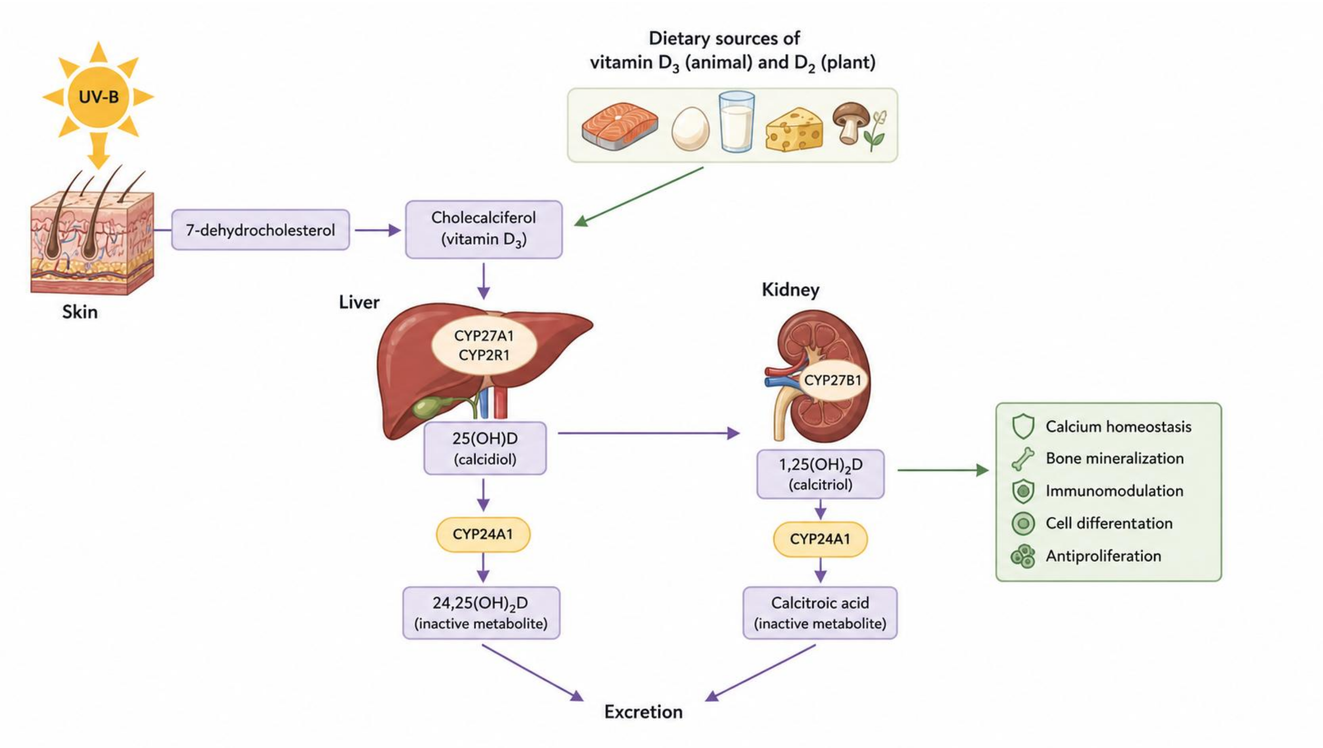

Figure 1: Normal vitamin D metabolism.

Vitamin D is obtained either through skin synthesis or dietary intake. In the skin, ultraviolet (UV) radiation converts 7-dehydrocholesterol into vitamin D_3 (cholecalciferol). It can also be derived from plant sterols (ergosterol) or consumed directly in the diet as vitamin D_3 or vitamin D_2 (ergocalciferol). Both forms are subsequently hydroxylated in the liver by cytochrome P450 enzyme CYP27A1 to form 25-hydroxyvitamin D (25(OH)D), also known as calcidiol or calcifediol. This metabolite is then further converted, primarily in the kidney, by 1α-hydroxylase (CYP27B1) into the biologically active form, 1,25-dihydroxyvitamin D (1,25$(OH)_2$D), also called calcitriol.

Source: authors' diagram

1.3. Vitamin D deficiency (VDD)

Vitamin D deficiency (VDD) may serve as a marker for systemic dysregulation, particularly in aging populations, as it has been repeatedly linked to a number of systemic health problems, such as cardiovascular disease, renal dysfunction, and increased all-cause mortality [1] [3] [8]. Interestingly, studies suggest that VDD can be a sign of underlying systemic health issues rather than a direct cause of poor health outcomes [1].

The implications of vitamin D status on eye health are gaining attention. Vitamin D may directly affect ocular tissues since the retina and optic nerve head express the vitamin D receptor (VDR) [3] [4]. Given vitamin D's known effects on inflammation and neuroprotection, a number of studies have examined the relationship between vitamin D levels and glaucoma risk [5] [4]. Understanding how vitamin D supplementation may affect disease trajectories in at-risk groups is crucial due to the complex interactions between vitamin D levels, systemic health, and the risk of developing glaucoma.

1.4. Vitamin D Supplementation

Vitamin D supplementation has gained significant attention due to its multifaceted role in human health, particularly in relation to eye health and the potential risk of developing glaucoma. Vitamin D, primarily in the form of 25-hydroxyvitamin D (25(OH)D), serves as a crucial biomarker for assessing vitamin D status and is involved in numerous biological functions including immune modulation, cellular proliferation, and neuroprotection within the central nervous system, including the optic nerve [5] [4].

1.5. Sources and Synthesis of Vitamin D

Humans acquire vitamin D through dietary sources and synthesis in the skin via exposure to ultraviolet B radiation. Natural dietary sources include fatty fish, egg yolk, and liver, while many foods, such as milk and cereals, are fortified with vitamin D2 (ergocalciferol) or D3 (cholecalciferol). Endogenously, vitamin D3 is produced in the skin and converted in the liver to 25-hydroxyvitamin D, which is further modified in the kidneys to its active form, calcitriol [4] [1].

2. Role of Vitamin D in Ocular Health

2.1. Effect on Intraocular Pressure (IOP)

Research indicates that vitamin D deficiency is associated with various neurodegenerative effects, particularly impacting the central nervous system. The optic nerve, which is essential for vision, is notably influenced by vitamin D levels, suggesting that adequate supplementation could potentially mitigate risks associated with glaucoma, a chronic progressive optic neuropathy characterized by irreversible damage [5] [3].

Vitamin D is increasingly recognized as a multifaceted regulator of ocular and systemic physiology, with potential implications for intraocular pressure (IOP) and glaucoma pathogenesis. Beyond its direct ocular effects, vitamin D contributes to the modulation of systemic conditions such as diabetes mellitus and arterial hypertension, both of which are established metabolic risk factors associated with elevated IOP and impaired ocular perfusion, thereby increasing susceptibility to glaucomatous damage. [4] [1].

Evidence regarding the relationship between vitamin D and IOP remains heterogeneous, encompassing both experimental and clinical observations. Preclinical studies have demonstrated that topical administration of calcitriol or its analogs in animal models, particularly in primates, can induce a substantial reduction in IOP - reaching up to approximately 20% - with effects persisting for over 12 hours. In parallel, several epidemiological and clinical investigations have identified an inverse correlation between serum vitamin D levels and IOP, suggesting that higher circulating concentrations of vitamin D may be associated with lower intraocular pressure. This relationship appears particularly notable in certain populations, including individuals of African descent, in whom lower vitamin D status has been linked to higher IOP values. [9]

However, findings from human interventional studies remain inconclusive. Some clinical trials have not demonstrated a significant reduction in IOP following systemic vitamin D supplementation, which may be attributable to the necessity of local intraocular conversion to the active metabolite, calcitriol, in order to exert biological effects within ocular tissues. Consequently, systemic vitamin D levels may not reliably reflect the bioactive concentrations required at the site of action. [9]

In addition to its potential role in IOP regulation, vitamin D exhibits neuroprotective properties that may be relevant in glaucoma. Through its anti-inflammatory and antioxidant actions, it is thought to confer protection to retinal ganglion cells and the optic nerve, thereby potentially mitigating the progression of glaucomatous optic neuropathy. [9,10]

2.2. Impact on Eye Drainage

1α,25-dihydroxyvitamin D3 (Calcitriol) has been demonstrated to reduce oxidative stress-induced damage in human trabecular meshwork (TM) cells by blocking the TGFβ-SMAD3-VDR pathway. Inhibiting this route, which is the principal regulator of extracellular matrix deposition in the TM, aids in preserving the drainage system's structural integrity and functionality under stress. [9] In addition, because of its natural antioxidant, immune-modulating, and anti-inflammatory qualities, vitamin D is thought to be essential for neuroprotection. [9] It contributes to the development of a more robust interior environment that can better shield delicate ocular tissues by lowering chronic inflammation. [10]

Moreover, research indicates that calcitriol may play a significant role in reducing intraocular pressure by modulating both the production and outflow of aqueous humor. The trabecular meshwork, which constitutes the principal drainage system of the eye, is thought to exhibit decreased resistance in the presence of vitamin D, a phenomenon mediated through several molecular mechanisms. One such mechanism involves extracellular matrix remodeling, whereby vitamin D regulates the expression of genes responsible for maintaining the structural integrity of the trabecular meshwork; specifically, it has been shown to upregulate matrix metalloproteinases (MMP-3, MMP-11, MMP-13, and MMP-14) while downregulating their inhibitor TIMP-3, thereby facilitating enhanced aqueous humor outflow.

Furthermore, calcitriol suppresses the expression of genes such as fibronectin I and RHOA (Ras homolog gene family, member A), both of which are associated with increased intraocular pressure. By inducing alterations in cellular architecture by downregulating genes involved in cell adhesion, such as CD44, as well as cytoskeletal components including α- and γ-actins, vitamin D may further reduce resistance to fluid drainage. [9]

2.3. Reduction of oxidative stress

Vitamin D supports cellular longevity by promoting telomere length, which may reduce the rate at which cells age making cellular processes more flexible and less vulnerable to the constant stress and oxidative damage linked to diseases like glaucoma. This promotes the long-term health of eye tissues. [10] Another property of vitamin D is that it can reduce oxidative stress by creating a "quiet, persistent defense" within the body. This may prevent the optic nerve and retinal ganglion cells from gradually deteriorating. [10] Although these preclinical results are encouraging, the authors emphasize the necessity for wider human clinical trials to completely confirm these protective effects and point out that the precise molecular pathways are still being investigated. [9]

2.4. Vitamin D and its protective properties

Furthermore, several preventive functions of vitamin D may have an impact on potential processes for the development of glaucoma, either directly through activation of the vitamin D receptor or indirectly through control of calcium homeostasis [13,16]. First, vitamin D may have an impact on immunomodulation in glaucoma etiology - neurodegenerative damage to the optic nerve axons and ganglion cell bodies is mainly triggered by an immune system imbalance. Vitamin D has a major impact on immune cell modulation, which may be crucial for safeguarding the optic nerve. [14]. According to recent research, vitamin D may have a number of preventive functions in the development of glaucoma, either directly through activation of the vitamin D receptor or indirectly through regulation of calcium homeostasis [13, 14].

Second, vitamin D controls neural network plasticity as well as neurotrophic factors in the central nervous system [11, 12]. Vitamin D has a neurotrophic property linked to neurotransmitter metabolism and the creation of neurotrophic growth factors, according to research employing animal models [11, 12]. This impact might help the injured optic nerve regenerate.

Third, vitamin D performs a significant role in glaucomatous optic nerve injury by modulating oxidative stress in neurons through the activation of calcium channels [13,14,15]. Numerous neurological and psychiatric conditions, including depression, schizophrenia, Parkinson's disease, and Alzheimer's disease, are strongly linked to vitamin D [13]. These conditions may have an influence on the development of glaucoma, according to several research [14]. Studies have shown that neurodegenerative damage to the optic nerve axons and ganglion cell bodies is largely caused by an immune system imbalance. Vitamin D has a major impact on immune cell modulation, which may be crucial for safeguarding the optic nerve.

Moreover, vitamin D controls neural network plasticity as well as neurotrophic factors in the central nervous system [11, 12]. Vitamin D has a neurotrophic property linked to neurotransmitter metabolism and the creation of neurotrophic growth factors, according to research employing animal models [11, 12]. This impact might help the injured optic nerve regenerate.

Additionally, vitamin D plays a significant role in glaucomatous optic nerve injury by controlling oxidative stress in neurons through the activation of calcium channels [13,14,15]. Especially its active form 1α,25-dihydroxyvitamin D3 (calcitriol), shields the eye against oxidative stress by TGFβ-SMAD3-VDR Pathway Inhibition. [9]

3. Considerations for Supplementation

While vitamin D supplementation can be beneficial, especially for individuals at risk of deficiency, it is crucial to tailor doses appropriately. The upper tolerable limit for oral supplementation is generally set at 4000 IU per day for healthy individuals, although those who are vitamin D deficient may require higher doses [3]. Caution is advised to prevent vitamin D toxicity, which can result from prolonged high-dose supplementation. Regular monitoring of serum vitamin D levels is recommended to ensure safety and efficacy in supplementation strategies aimed at preventing glaucoma[4] [3] [1].

4. Research Studies

4.1. Vitamin D and Ocular Health regarding to sex-based differences

To begin with, recent research has explored the association between vitamin D levels and ocular health, particularly in relation to open-angle glaucoma (OAG). A study observed no significant trend between vitamin D levels and OAG in females, suggesting that menstrual status or hormone replacement therapy may influence this relationship. After menopause, women experience lower levels of estrogen and progesterone, which could be an independent risk factor for developing OAG, unlike men who do not face this hormonal decline [4]. Furthermore, it has been suggested that sexual hormonal status could lead to nutritional deficiencies and various chronic diseases, potentially linking low vitamin D levels to the development of OAG [4].

Research into the link between vitamin D and OAG has often produced conflicting results regarding sex-based differences. One cross-sectional study of 6,094 South Korean participants reported an inverse association between serum 25(OH)D concentration and OAG in males only. Conversely, a much larger retrospective study of 123,331 South Korean participants found that lower vitamin D levels were significantly associated with an elevated risk of glaucoma in females only. Notably, the study that found a link in females also reported no association between vitamin D and intraocular pressure (IOP). This suggests that in women, vitamin D may influence glaucoma through pathways other than pressure regulation, such as direct neuroprotection of the optic nerve. [17,18,19]

Based on other studies, the link between hormonal levels and OAG can be considered as an independent risk factor for the development of OAG due to the decline in estrogen and progesterone after menopause. This distinguishes the risk profile of women from that of men, who do not undergo a similar dramatic hormonal drop. It has been proposed that this hormonal change may potentially contribute to nutritional inadequacies that further aggravate disease risk. Lower 25(OH)D levels were significantly linked to an increased risk of glaucoma in females only, according to a larger retrospective cross-sectional study of 123,331 South Korean participants [9]. No correlation was found between IOP and vitamin D, suggesting that vitamin D may play a role in glaucoma pathogenesis independent of IOP levels. The number of female and male subjects in their research population, however, varied greatly, and the group with high IOP was much smaller than the group with normal IOP. Furthermore, fundus photos alone - without any gonioscopic description of the angle - were used to diagnose the participants with glaucoma. This reduces the validity of the presumptive patient classification and, thus, the conclusions about the correlation between vitamin D and glaucoma risk. [35] Nevertheless, this can potentially be a critical finding because it suggests that in women, the protective effects of Vitamin D and potentially its interaction with estrogen occur through direct neuroprotection of the optic nerve rather than through fluid drainage regulation.

Secondly, vitamin D is known for its anti-inflammatory and antioxidant properties, which help protect retinal ganglion cells from oxidative stress. The sources suggest that the lack of these protective factors, potentially exacerbated by low estrogen levels, could explain the development or severity of OAG in certain patients, This conclusion was presented in an American case-control study in a cohort of 357 POAG patients of African descent [36].

In elderly populations vitamin D deficiency has been linked to a reduced macular ganglion cell complex (GCC), a sign of neuronal loss that can precede the visible thinning of the retinal nerve fiber layer seen in glaucoma. With aging the ability where the body can absorb essential nutrients decreases. Older adults frequently face "nutrient gaps" in Vitamin D and B12, both of which are vital for nerve and vascular support. These gaps, combined with systemic hormonal changes, can leave the eyes and nerves more exposed to the "unrelenting" damage associated with OAG.

In summary, the sources indicate that for women, the risk of OAG is tied to a complex interplay of hormonal decline and nutrient status that affects the longevity and resilience of the optic nerve independently of eye pressure. [9,10]

4.2. The link between vitamin D and glaucoma severity

Research into the link between vitamin D and glaucoma severity has yielded mixed results, with some studies suggesting a strong correlation while others find no significant relationship.

4.2.1. Evidence Supporting a Link to Severity

An American case-control study focusing on individuals of African descent found that serum levels of 25-hydroxyvitamin D (25(OH)D) were significantly lower in patients with advanced glaucoma (visual field loss worse than −10 dB) compared to those with early-stage glaucoma or healthy controls. [36] Vitamin D deficiency has also been associated with a reduced macular ganglion cell complex (GCC) thickness. This neuronal loss in the GCC may represent an early stage of neurodegeneration that precedes the thinning of the retinal nerve fiber layer typically seen in progressing glaucoma. [37-40] Recent findings suggest that optimal vitamin D levels may support telomere length and reduce chronic inflammation, which could slow cellular aging and help the optic nerve resist the gradual, unrelenting damage seen in severe glaucoma. [10]

4.2.2. Conflicting Clinical Data

Despite the findings above, other studies have failed to establish a clear link between vitamin D and disease progression. A French population case-control study found that while glaucoma patients generally had lower vitamin D levels than healthy individuals, there was no statistical difference in serum concentrations between patients with moderate and severe primary open-angle glaucoma (POAG). Serum 25-hydroxyvitamin D [25(OH)D] levels were not found to be associated with intraocular pressure or visual field mean deviation in the studied cohort. However, interpretation of these findings is limited, as patients with primary open-angle glaucoma (POAG) were undergoing treatment to control IOP, which may have obscured any potential pressure-lowering effects of vitamin D. Vitamin D supplementation was assessed based on self-reported use, without detailed information regarding dosage, regimen, route of administration, or duration. Although supplementation was included as a covariate in the statistical analysis, the lack of precise data restricts meaningful conclusions about its impact on the outcomes. Additionally, the study’s case-control design and relatively small sample size further limit the strength and generalizability of the findings. [41]

In summary, while some evidence suggests that vitamin D deficiency may exacerbate glaucoma severity by reducing neuroprotection and accelerating neuronal loss, the scientific community emphasizes the need for larger, randomized controlled trials to confirm if vitamin D supplementation can effectively slow disease progression.

4.3. Genetic Analysis and Vitamin D

Mendelian randomization (MR) analysis has been utilized to assess the causal relationship between vitamin D levels and eye conditions. This approach minimizes confounding factors typically present in observational studies. Despite the strengths of MR design, including a robust sample size that provides reliable causal relationships, it is important to note limitations, such as the predominance of genetic instruments from European populations, which may not be applicable to other ethnic groups. The complex biological pathways associated with vitamin D may also limit the generalizability of findings to broader populations [42].

4.4. Future Research Directions

There is a call for further longitudinal studies to investigate the potential impact of vitamin D supplementation on glaucoma progression. Such studies could clarify the role of vitamin D in ocular health and its therapeutic potential in preventing or managing glaucoma The systematic review of existing literature aims to summarize current knowledge on vitamin D's effects on eye diseases, highlighting the necessity for ongoing research in this area [6].

Discussion

Vitamin D has garnered significant interest for its potential role in ocular health, particularly concerning diseases such as glaucoma. Recent studies indicate that vitamin D may exert protective effects against various ocular conditions through its regulatory influence on immune response and cellular behavior within the eye [3]. The presence of the vitamin D receptor (VDR) in ocular tissues underscores the nutrient's importance in maintaining ocular homeostasis and suggests that vitamin D deficiency (VDD) could correlate with adverse outcomes in eye diseases, including glaucoma [6] [3]. The intersection of vitamin D and ocular health is particularly evident in conditions characterized by inflammation and cellular remodeling, such as dry eye disease and keratoconus, both of which are implicated in glaucoma pathogenesis [3] [4]. Vitamin D's anti-inflammatory properties may mitigate ocular surface inflammation, a contributing factor to various eye disorders, enhancing the overall health of the eye and potentially reducing the risk of glaucoma development [3]. Moreover, emerging evidence suggests that VDD may correlate with increased risks of systemic health issues, such as cardiovascular disease and renal dysfunction, which are known to influence glaucoma outcomes [1] [3]. The interaction between vitamin D pathways and the TGFβ signaling pathway offers further insight into the mechanisms by which vitamin D may impact myofibroblast-like cells, such as those in the trabecular meshwork. The VDR-RXR heterodimer may act as a competitive antagonist to SMAD3 binding, inhibiting the transcription of profibrotic factors that contribute to fibrosis and increased intraocular pressure, key components in glaucoma pathology [3]. This regulatory role of vitamin D could represent a therapeutic target, where maintaining sufficient vitamin D levels might aid in preventing the progression of glaucomatous damage. However, the current literature is not without its contradictions, and further research is warranted to clarify the relationship between vitamin D status and glaucoma risk. While some studies suggest a protective effect of adequate vitamin D levels, others do not find a clear association [6] [4]. This variability may be attributed to differences in study design, population characteristics, and the complex interplay of vitamin D with other systemic factors affecting ocular health.

Conclusions

Vitamin D supplementation and its potential relationship with the risk of developing glaucoma has become a significant focus of research due to the nutrient's extensive role in systemic health and ocular function. Glaucoma, a chronic and progressive optic neuropathy, is a leading cause of irreversible blindness worldwide, with projections estimating the number of affected individuals to rise from 76 million in 2020 to 111.8 million by 2040. [1] [2] The condition primarily impacts older adults, many of whom also manage other chronic diseases, underscoring the importance of understanding factors that may influence its onset and progression. Vitamin D is recognized for its crucial role in various biological processes, including immune modulation, cellular differentiation, and neuroprotection, particularly within the central nervous system.[3] [4]

Vitamin D deficiency (VDD) has been linked to multiple health issues, raising interest in its potential impact on ocular health. The vitamin D receptor (VDR) is expressed in the retina and optic nerve head, suggesting that adequate vitamin D levels might play a protective role against glaucoma by influencing inflammation and neurodegenerative processes.[5] [3]

Research has produced mixed results regarding the relationship between vitamin D levels and glaucoma risk. Some studies indicate that adequate vitamin D may help mitigate the effects of systemic health issues, such as hypertension and diabetes, which are known risk factors for elevated intraocular pressure and, consequently, glaucoma development.[4] [1]

However, other studies have failed to find a consistent association, suggesting that the relationship may be influenced by hormonal status, genetic factors, and broader systemic health challenges.[4] [6]

As research continues, the question of how vitamin D supplementation may affect glaucoma risk remains crucial, with calls for further longitudinal studies to clarify its potential therapeutic benefits and inform clinical practices.[6] The complexities surrounding vitamin D, its systemic implications, and its specific effects on ocular health highlight a compelling area of investigation, with ongoing debates about its role in the prevention and management of glaucoma.

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2. Data were obtained from pages PubMed and Google Scholar.

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