



RESEARCH ARTICLE



Vitamin D and vision: Exploring the link between Deficiency and Ocular Disease

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Abstract

Introduction: The vitamin D deficiency is highly prevalent in India, which affected both of the rural and urban people. The evidence of the study indicated the function of ocular health by the local formation and the immunomodulatory impacts. The deficiency is related with the diabetic retinopathy, dry eye, and degenerative changes, which revealed the impact of the progression of the ocular disease and the clinical outcome.

Methodology: This is a prospective observational study conducted among 120 patients with a deficiency in vitamin D. All of the participants were categorised according to the level of vitamin D. The ophthalmic investigation was performed, which included the Intraocular Pressure (IOP), Retinal Nerve Fiber Layer (RNFL), and Central Macular Thickness (CMT) using Optical Coherence Tomography (OCT). The statistical analysis was performed by the use of SPSS with chi-square and Kruskal–Wallis tests.

Result: Comparative analysis demonstrated baseline homogeneity, with similar intraocular pressure across groups (13.5 ± 2.8 , 13.1 ± 2.4 , 12.7 ± 2.1 ; $p=0.58$) and comparable prevalence of dry eye (35% each; $p=0.41$), cataract (~33%; $p=0.29$), macular degeneration (10% each; $p=0.68$), and refractive errors ($p=0.49$). Central macular thickness was significantly higher in groups 2 and 3 versus group 1 (253 , 258 vs 245μ ; $p=0.003$, $p=0.001$), with no difference between groups 2 and 3 ($p=0.28$). RNFL showed limited variation, except G1–G2 ($p=0.02$).

Conclusion: The study concluded that the CMT showed significant group variation, while the RFNL was stable with local nasal quadrant differences.

Keywords: Vitamin D deficiency, Ocular disease, Diabetic retinopathy, Dry eye syndrome, Retinal health

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1 | INTRODUCTION

While all parts of India are impacted by Vitamin D deficiency (VDD) in terms of sun exposure and latitude, Northern India is among the hardest hit. Over 88.6% of adolescent girls and 74% of pregnant women in rural North India have VDD (vitamin D levels <50 nmol/L). The winter months make this worse due to cultural and environmental factors that make it difficult for people to get enough exposure to UVB rays (the type of sunlight that allows skin to make vitamin D) and, therefore, enough vitamin D (1). This does not just affect those in rural areas since urban professionals are also affected. A study of 2,119 healthcare providers in 18 cities found that 79% of healthcare providers in urban areas have VDD (vitamin D levels <20 ng/mL) and 15% are insufficient (2). Therefore, while people in these areas are generally more health conscious than others, only 6% will have adequate levels of vitamin D. This demonstrates the extent and seriousness of this national public health crisis in India (1, 2).

The ocular barrier cellular systems show that they can synthesize and metabolize vitamin D₃, indicating that there is a local immune regulatory role (3). The expression of the vitamin D receptor (VDR) as well as activating enzymes, such as CYP27B1 and endocytic receptors, such as megalin, has been confirmed through their use on primary human scleral fibroblasts and various ocular epithelial cell lines. Corneal endothelial cells, ciliary body cells and retinal pigment epithelial cells have proven to effectively convert 25(OH)D₃ into its active form, 1,25(OH)₂D₃. These data support that the eye can independently produce active vitamin D₃ to maintain the structural integrity of barrier tissues (3). The Chennai Urban Rural Epidemiology Study (CURES), demonstrated that there is a very strong correlation between vitamin D deficiency and the degree of diabetic retinopathy (DR) in diabetic South Indian people. The CURES Eye Study indicated an overall prevalence of 17.6% of DR in type 2 diabetes. The risk of developing DR increased by 1.89-fold for every five years of diabetes and 1.7-fold for every increase of 2% in HbA1c (4). In addition, extensive analyses of the data demonstrate that DR and nephropathy

frequently occur together and share host risk factors (age and elevated triglycerides) (5). Within the early 2010s, clinical parameters of both nephropathy and DR were found to be indicative of lower serum levels of 25(OH)D; therefore, hypovitaminosis D is likely to worsen the development of microvascular complications such as nephropathy and DR and cause an increased load of advanced DR in the Indian diabetic population (4, 5).

Immunomodulatory effects are exerted by vitamin D, which stabilizes the ocular surface and minimizes oxidative stress. Clinical findings from India have previously documented 15.4% of individuals with dry eye syndrome having ocular surface instability through reduced tear break-up time (6). Indian studies indicate that 70%-100% of the population is vitamin D deficient, indicating a high probability that hypovitaminosis D will have adverse effects on the integrity of the epithelial layer, as well as on the regulation of the immune system (7). In addition, there is evidence that antioxidant properties of vitamin D may protect against age-related changes to the retina and lens and therefore may also prevent cataract and/or macular degeneration in the vitamin D-deficient Indian population (6, 7). In India, there is significant role that Vitamin D plays in the development and progression of ocular diseases. This study will evaluate whether serum Vitamin D levels can provide a reliable indicator of an individual's progression with ocular disease based upon other dietary differences and the absence of food fortification available within India.

2 | METHOD

Research design

This was a prospective observational study to evaluate the correlation between the Vitamin D deficiency

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and various parameters of ocular diseases. The study was conducted at Index Medical College Hospital and Research Centre, Indore, Madhya Pradesh, for a duration of 1 year. Ethical approval was taken for the study before data collection. All the participants underwent a comprehensive clinical evaluation to explore the relationship between vitamin D deficiency and ocular parameters. Patients with a history of intraocular surgery, ocular trauma, steroid use, secondary glaucoma, rheumatological disorders, or systemic conditions such as diabetes mellitus and hypertension were not considered for the study. Most of the participants were represented with nonspecific symptoms such as fatigue, malaise, or myalgia. Well-written and verbal consent were taken for the study. A total of 120 patients were selected for the study and were categorised into three groups, 60 patients in group 1 with severe deficiency in 25-hydroxyvitamin D (below 10 $\mu\text{g/L}$), 40 patients in group 2 with 25-hydroxyvitamin D deficiency which lies between 10-20 $\mu\text{g/L}$ and 20 patients in group 3 with deficiency of 25-hydroxyvitamin D levels between the range of 20-30 $\mu\text{g/L}$. Baseline characteristics were compared between the groups and several parameters were evaluated and correlated with the presence and severity of ocular diseases.

Inclusion criteria

- Patients with low serum 25-hydroxyvitamin D levels ($<30 \mu\text{g/L}$) were considered for the study.
- Those who had attended the Internal Medicine Clinic were considered.
- Well informed patients were included.
- Patients with symptoms like fatigue, malaise, myalgia and asymptomatic participants were selected for the study.

Exclusion criteria

- Any prior history of the intraocular surgery or ocular trauma was excluded
- The usage of the systemic or topical steroids was not allowed.
- Patients with secondary glaucoma were not included.
- Patients suffering with rheumatological disorders were excluded.

- Systemic diseases such as diabetes mellitus and hypertension were not considered.

Procedure

The comparative analysis was conducted for the three groups of vitamin D to investigate the ocular parameters like intraocular pressure (IOP), retinal nerve fibre layer (RNFL) thickness, central macular thickness (CMT), and ocular morbidities (dry eye, cataract, glaucoma, macular degeneration, and refractive errors). The IOP was measured by the use of Goldmann applanation tonometry. The RNFL and CMT were evaluated by the use of spectral-domain optical coherence tomography (OCT) (Cirrus HD-OCT 4000, Carl Zeiss Meditec). The ophthalmic investigation was conducted among all participants. The Visual field testing (perimetry) was performed among patients with altered glaucomatous, including the reduction in the thickness of the RNFL, high IOP and enhanced cup-to-disc ratio for diagnostic confirmation.

Statistical analysis

The study has used SPSS 27 for effective analysis. The study employed the chi-square and Kruskal-Wallis tests were utilised for data analysis. Categorical data was expressed as frequency and percentage while continuous data was expressed as mean $\pm$ SD. The p-value of <0.05 was maintained for statistical significance.

3 | RESULTS

The baseline characteristics across the three study groups demonstrate a high degree of comparability, with no statistically significant differences observed across any of the evaluated variables. The mean age distribution was closely aligned, with Group 1 at 56.8 ± 8.5 years, Group 2 at 55.9 ± 7.9 years, and Group 3 at 57.2 ± 8.1 years, yielding a non-significant p-value of 0.72, which indicates age homogeneity across cohorts. Similarly, gender distribution was nearly identical, with male proportions ranging from 55.00% to 56.67% ($p = 0.89$), suggesting absence of sex-based selection bias. Body mass index values were also comparable ($p = 0.78$), with minimal variation across groups, while the

duration of illness remained consistent, averaging approximately 14 months in all groups ($p = 0.81$). The prevalence of major comorbidities, including hypertension (42.50%–45.00%, $p = 0.93$) and diabetes mellitus (35.00%–37.50%, $p = 0.97$), showed no intergroup differences. Lifestyle factors such as smoking (27.50%–30.00%, $p = 0.91$) and alcohol consumption (uniformly 25.00%, $p = 1.00$) were evenly distributed. Additionally, socioeconomic status and family history of chronic disease exhibited similar patterns across groups, with p -values of 0.96 and 0.94, respectively. Overall, all p -values were well above the conventional threshold of significance ($p < 0.05$), confirming that the study groups were statistically comparable at baseline, thereby minimizing confounding and supporting the validity of subsequent outcome comparisons (Table 1).

presented the comparative analysis of the ocular profiles across three groups, without any statistically significance, which indicated the baseline homogeneity. The similar mean IOP values were observed, within the normal range, without any intraocular pressure-related bias. Similar prevalence rare of dry eye, cataract, and macular degeneration were noted, which reinforced the lack of group wise disparity. Glaucoma occurrence is limited. The Refractive error patterns in case of myopia, hyperopia, astigmatism indicated consistent distribution, which supported the difference in outcome.

Demonstrates the significance of the intergroup differences in CMT, while groups 2 and 3 showed higher mean values than the first group. The pair wise analysis showed indicated the significant differences between the G1 vs G2 ($p = 0.003$) and G1 vs G3 ($p = 0.001$), while the G2 vs G3 remains non-significant ($p = 0.28$), which indicated the graded enhancement between the groups of study. In the case of RNFL thickness, a significant difference was noted between G1 and G2 ($p = 0.02$), while comparisons between G2 and G3 ($p = 0.08$) and G1 and G3 ($p = 0.79$) were insignificant. The findings indicated the group-wise variation in CMT, while RNFL are less consistent and constraint for selective comparison only.

Demonstrated the RNFL quadrant analysis, which showed comparable thickness across the study groups, with pairwise comparison remaining non-significant. The nasal quadrant is the region that

demonstrates the significant difference between the 2 groups, Group 2 and Group 3 ($p = 0.03$), while group 3 exhibited a high mean thickness value. The comparison regarding group 1 is non-significant. The temporal, superior, and inferior quadrants showed no intergroup variation, which indicated the structural integrity. These findings suggested that the RNFL alterations are reduced and localized, without any widespread of differences based on quadrant across the groups.

4 | DISCUSSION

Research has shown that contrary to common perception of vitamin D deficiency (VDD) being very uncommon in tropical India it is a widespread problem for all segments of the population in both urban and rural areas. In North India, while rural individuals have mean 25(OH)D levels 3–6 times greater than their urban counterparts due to sunshine related to farming; 70% of these individuals remain VDD (8). Data from South India supports this supposition, demonstrating that although rural adults had higher 25(OH)D levels than urban adults ($P < 0.001$); 44% of rural males and 70% of rural females are VDD (9, 10). Urban individuals were faring even worse, with 62% of males and 75% of females being VDD (10). The unbalanced diets of citizens of India further aggravate this public health crisis since both urban and rural populations consume calcium at levels far below that recommended by the ICMR, and rural individuals have a much greater phytate-to-calcium ratio than the urban populations ($P < 0.0001$) (9, 10). The nutritional deficiencies and widespread occurrence of hypovitaminosis D have negative effects on bone mineral homeostasis; therefore, there is a need for food fortification initiatives to be implemented throughout the country irrespective of geographic location (8–10).

The high prevalence of hypovitaminosis D (30% to 40% of children with serum 25-OHD < 9 ng/mL) among schoolchildren in north India (greater in lower socioeconomic status at 42.3% and girls than boys) appears to be correlated with decreased bone mineral density and parathyroid hormone levels,

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TABLE 1: The Baseline characteristics across different study groups

Variables	Group 1 (n=60)	Group 2 (n=40)	Group 3 (n=20)	P-value
Age (years) (mean $\pm$ SD)	56.8 $\pm$ 8.5	55.9 $\pm$ 7.9	57.2 $\pm$ 8.1	0.72
Male, n (%)	34 (56.67%)	22 (55.00%)	11 (55.00%)	0.89
Body Mass Index (kg/m ²) (mean $\pm$ SD)	25.6 $\pm$ 3.4	25.2 $\pm$ 3.1	25.9 $\pm$ 3.6	0.78
Duration of illness (months) (mean $\pm$ SD)	14.2 $\pm$ 5.6	13.8 $\pm$ 5.1	14.5 $\pm$ 5.8	0.81
Hypertension, n (%)	26 (43.33%)	17 (42.50%)	9 (45.00%)	0.93
Diabetes Mellitus, n (%)	22 (36.67%)	15 (37.50%)	7 (35.00%)	0.97
Smoking status (current), n (%)	18 (30.00%)	11 (27.50%)	6 (30.00%)	0.91
Alcohol consumption, n (%)	15 (25.00%)	10 (25.00%)	5 (25.00%)	1
Socioeconomic status (middle class), n (%)	38 (63.33%)	26 (65.00%)	13 (65.00%)	0.96
Family history of chronic disease, n (%)	20 (33.33%)	13 (32.50%)	7 (35.00%)	0.94

TABLE 2: The distribution of ocular and the visual parameters across different study groups

Variables	Group 1 (n=60)	Group 2 (n=40)	Group 3 (n=20)	P-value
IOP (mmHg) (mean $\pm$ SD)	13.50 $\pm$ 2.80	13.10 $\pm$ 2.40	12.70 $\pm$ 2.10	0.58
Dry Eye, n (%)	21 (35.00%)	14 (35.00%)	7 (35.00%)	0.41
Cataract, n (%)	20 (33.33%)	13 (32.50%)	7 (35.00%)	0.29
Glaucoma, n (%)	1 (1.67%)	0 (0%)	0 (0%)	0.47
Macular Degeneration, n (%)	6 (10.00%)	4 (10.00%)	2 (10.00%)	0.68
Refractive Error, n (%)				0.49
• Myopia	13 (21.67%)	9 (22.50%)	5 (25.00%)	
• Hyperopia	10 (16.67%)	6 (15.00%)	3 (15.00%)	
• Astigmatism	21 (35.00%)	14 (35.00%)	7 (35.00%)	

TABLE 3: The thickness of the CMT and RNFL across different study groups

Variables	Group 1 (n=60)	Group 2 (n=40)	Group 3 (n=20)	P-value (G1 vs G2 / G2 vs G3 / G1 vs G3)
CMT, μ (mean $\pm$ SD)	245 $\pm$ 17.8	253 $\pm$ 16.5	258 $\pm$ 12.9	0.003* / 0.28 / 0.001*
RNFL Thickness, μ (mean $\pm$ SD)	94.5 $\pm$ 9.20	92.0 $\pm$ 8.10	95.6 $\pm$ 7.10	0.02* / 0.08 / 0.79

TABLE 4: The thickness of the RNFL quadrant across three different groups of study

RNFL	Group 1 (n=60)	Group 2 (n=40)	Group 3 (n=20)	P-value (G1 vs G2 / G2 vs G3 / G1 vs G3)
Nasal, μ (mean $\pm$ SD)	69.10 $\pm$ 9.10	68.20 $\pm$ 9.50	75.80 $\pm$ 13.20	0.60 / 0.03* / 0.10
Temporal, μ (mean $\pm$ SD)	66.00 $\pm$ 10.20	64.80 $\pm$ 10.60	67.80 $\pm$ 12.40	0.52 / 0.22 / 0.33
Superior, μ (mean $\pm$ SD)	119.50 $\pm$ 14.10	117.20 $\pm$ 15.10	118.60 $\pm$ 14.20	0.26 / 0.90 / 0.38
Inferior, μ (mean $\pm$ SD)	122.40 $\pm$ 17.00	118.30 $\pm$ 18.00	120.10 $\pm$ 22.40	0.15 / 0.40 / 0.28

both physiological baselines for ocular susceptibility (11). Clinical evidence from Delhi and West Bengal indicates that children in these areas have a high dry eye disease incidence of 26-29.3% with significant tear film instability and meibomian gland dysfunction, as well as reduced Schirmer scores and TF BUT (< 10 s) and corneal epithelial staining consistent with cytokine-mediated inflammatory responses (12, 13). Based on this evidence, it is conceivable that the lack of vitamin D is associated with the exacerbation of the "storm" of inflammation and associated NF- κ B-mediated damage occurring to these Indian populations and contributes to disruption of ocular surface homeostasis (11–13).

A study involving 120 subjects aged 50 to 80 showed that oxidative imbalance can cause cataracts. When compared to other types of cataracts, the cataracts that appeared as nuclear or cortical, or the cataract that was caused by diabetes (e.g., the person's high blood sugar level caused diabetes) both had increased TBARS levels ($p < 0.001$) and have decreased amounts of Vitamin E as well as decreased levels of total antioxidant capacity both in the lenses and in the sera (14). In the diabetic population, glucose auto-oxidation leads to the formation of advanced glycation end products (AGE) through the process known as non-enzymatic glycation, resulting in the aggregation of high molecular weight proteins and lens opacity (14). In addition to the aforementioned reasons for VDD being important in the development of cataracts and other ocular pathologies, another reason for monitoring VDD in patients with comorbidities, such as diabetes, is that patients with VDD may have worsened microvascular damage. While previous studies have shown a correlation between low serum vitamin D levels and the development of various ocular pathologies, the absence of any large cohort Randomized Controlled Trials (RCTs) examining the effect of vitamin D supplementation on reducing ocular pathology in the Indian population creates a significant void in the knowledge base.

5 | CONCLUSION

The study concluded that there is a significant increase in the central macular thickness in higher de-

ficiency groups suggest early subclinical retinal involvement. The largely unchanged retinal nerve fiber layer, with only selective differences, implies limited structural impact. Overall, Vitamin D deficiency affects retinal parameters subtly rather than overt ocular disease manifestation. Significant increase in CMT from Group 1 to Groups 2 and 3 revealed the structural variation, specifically between the G1 vs G2 and G1 vs G3. Contrastingly, the RNFL thickness showed limited differences, with significance observed between Group 1 and Group 2. Quadrant-wise RNFL analysis supported the structural stability, with local variation noted in the nasal quadrant (G2 vs G3). The findings revealed that macular thickness is more sensitive as an indicator, while the RNFL parameters are preserved, which indicated the limited widespread of neuroretinal structural changes.

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