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Association Of Serum Vitamin D Levels With Dry Eye Disease: A Cross-Sectional Study From A Tertiary Centre In Manipur, Northeast India

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Abstract
Purpose: *To assess serum 25-hydroxyvitamin D [25(OH)D] levels in patients with dry eye disease (DED) and evaluate the association between vitamin D status and Schirmer I test values in a tertiary-care population from Northeast India.*
Methods: *This hospital-based cross-sectional study enrolled 140 adults with DED at RIMS, Imphal, between May 2022 and July 2024. Clinical evaluation included visual acuity, slit-lamp examination, intraocular pressure measurement, and Schirmer I testing without topical anaesthesia. Serum 25(OH)D was measured using an ELISA-based immunoassay. Vitamin D deficiency was defined as <20 ng/mL. Continuous and categorical variables were compared using the independent-samples t-test and chi-square test, respectively; $p < 0.05$ was considered statistically significant.*
Results: *Thirteen participants (9.3%) were vitamin D deficient and 127 (90.7%) were non-deficient. Mean Schirmer I values did not differ significantly between deficient and non-deficient groups (OD: 6.00 ± 1.63 vs 6.29 ± 1.67 mm, $p = 0.550$; OS: 6.23 ± 1.69 vs 6.49 ± 1.69 mm, $p = 0.602$). Unaided visual acuity, best-corrected visual acuity, and intraocular pressure were also comparable. Lower systolic and diastolic blood pressures were reported in the vitamin D-deficient group ($p = 0.008$ and $p = 0.047$, respectively).*
Conclusion: *Vitamin D deficiency was uncommon and was not associated with lower Schirmer I values in this cohort. The small deficient subgroup and reliance on Schirmer I testing alone limit interpretation. Larger studies using comprehensive dry-eye metrics are warranted.*
Keywords: *dry eye disease; vitamin D; Schirmer I test; tear production; 25-hydroxyvitamin D; Northeast India.*

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I. Introduction

Dry eye disease (DED) is a multifactorial ocular-surface disorder in which loss of tear-film homeostasis is accompanied by ocular symptoms; tear-film instability, hyperosmolarity, inflammation, ocular-surface damage, and neurosensory abnormalities may contribute to its pathogenesis [1]. DED is common, can impair visual function and quality of life, and has a substantial clinical burden [2,3].

Vitamin D has immunomodulatory and anti-inflammatory effects, and low serum 25(OH)D has been investigated as a possible contributor to ocular-surface dysfunction. Several observational studies have reported associations between vitamin D deficiency and DED or abnormal tear-film parameters [4-7]. In contrast, other population-based studies have not demonstrated a significant association [8,9]. Systematic reviews have therefore described substantial heterogeneity across populations, diagnostic definitions, and outcome measures [10,11].

Data from Northeast India remain limited. This study aimed to evaluate serum 25(OH)D status in adults with DED attending a tertiary centre in Manipur and to determine whether vitamin D deficiency was associated with differences in Schirmer I test values.

II. Methods

Study design and setting

This hospital-based cross-sectional study was conducted in the Department of Ophthalmology, Regional Institute of Medical Sciences (RIMS), Imphal, Manipur, from May 2022 to July 2024. Institutional Ethics Committee approval was obtained before recruitment, and written informed consent was obtained from all participants.

Study population

Inclusion criteria

- Adults aged ≥18 years.
- Clinically diagnosed dry eye disease based on symptoms and slit-lamp examination.
- Ability to undergo Schirmer I testing and venous blood sampling.

Exclusion criteria

Participants were excluded for any of the following:

- History of ocular trauma or ocular surgery.
- Use of topical ophthalmic medication during the preceding 3 months.
- Contact-lens wear.
- Eyelid disorders, including entropion, ectropion, or lagophthalmos.
- Allergic conjunctivitis or active ocular-surface infection.
- Meibomian gland dysfunction.
- Glaucoma, uveitis, or retinal pathology.
- Systemic autoimmune disease, including rheumatoid arthritis or Sjögren syndrome.
- Diabetes mellitus, thyroid disease, renal disease, malignancy, or neurological disease.
- Pregnancy, lactation, or severe malnutrition.

Clinical evaluation

All participants underwent the following examinations:

- Unaided and best-corrected visual acuity (BCVA) assessment using a Snellen chart.
- Slit-lamp examination of the anterior segment.
- Intraocular pressure (IOP) measurement by Goldmann applanation tonometry.

Schirmer I test

The Schirmer I test was performed without topical anaesthesia. Whatman No. 41 filter-paper strips were placed at the junction of the lateral and middle thirds of the lower eyelid margin. Tear wetting was recorded after 5 minutes. Values <10 mm/5 min were interpreted as reduced tear production.

Serum vitamin D estimation

A 3-mL venous blood sample was collected from each participant. Serum 25(OH)D concentration was measured using a standard ELISA-based immunoassay. Participants were classified as vitamin D deficient (<20 ng/mL) or non-deficient (≥20 ng/mL). This binary grouping was used for the planned statistical comparison.

Outcome measures

- Primary outcome: association between vitamin D category (deficient vs non-deficient) and Schirmer I test values.
- Secondary outcomes: differences in unaided visual acuity, BCVA, IOP, and systolic and diastolic blood pressure between vitamin D groups.

Statistical analysis

Data were analysed using IBM SPSS Statistics version 27. Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables as frequencies and percentages. Between-group comparisons used the independent-samples t-test for continuous variables and the chi-square test for categorical variables. A two-sided p-value <0.05 was considered statistically significant.

Ethics

The study was conducted in accordance with the Declaration of Helsinki. Approval was obtained from the Institutional Ethics Committee of RIMS, Imphal, and written informed consent was obtained from all participants.

III. Results

A total of 140 participants with DED were enrolled. The mean age was 41.6 ± 12.4 years; the largest age group was 31-40 years. Ninety-one participants (65.0%) were male, and 122 (87.1%) resided in urban areas (Table 1).

Table 1. Demographic characteristics of study participants (N = 140)

Variable	Category	Frequency (n)	Percentage (%)
Age group (years)	18-30	28	20.0
Age group (years)	31-40	45	32.1
Age group (years)	41-50	31	22.1
Age group (years)	51-60	20	14.3
Age group (years)	61-70	10	7.1
Age group (years)	>70	6	4.3
Sex	Male	91	65.0
Sex	Female	49	35.0
Locality	Urban	122	87.1
Locality	Rural	18	12.9

Serum vitamin D status

Thirteen participants (9.3%) were vitamin D deficient and 127 (90.7%) were non-deficient (Figure 1).

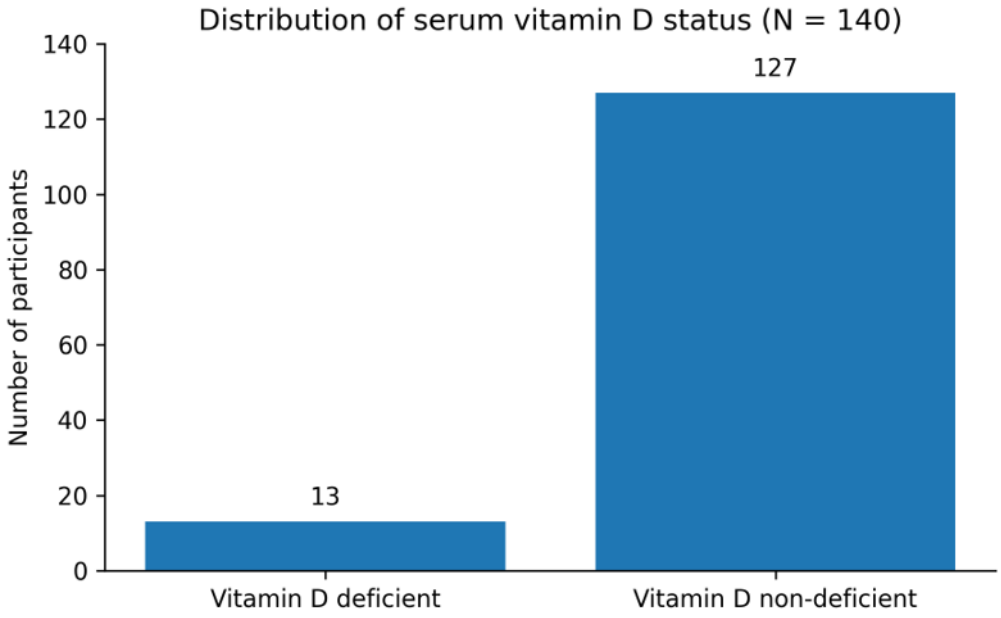

Figure 1. Distribution of serum vitamin D status among study participants.

Schirmer I test values

Mean Schirmer I values did not differ significantly between vitamin D-deficient and non-deficient groups in either eye (Table 2).

Table 2. Schirmer I test values by vitamin D status

Parameter	Vitamin D deficient, mean ± SD	Vitamin D non-deficient, mean ± SD	p-value
Schirmer I, OD (mm/5 min)	6.00 ± 1.63	6.29 ± 1.67	0.550
Schirmer I, OS (mm/5 min)	6.23 ± 1.69	6.49 ± 1.69	0.602

Visual acuity and intraocular pressure

Unaided visual acuity, BCVA, and IOP were comparable between vitamin D groups (Table 3). Visual acuity values are presented in the notation used in the source dataset.

Table 3. Visual acuity and intraocular pressure by vitamin D status

Parameter	Vitamin D deficient, mean ± SD	Vitamin D non-deficient, mean ± SD	p-value
Unaided VA, OD	0.65 ± 0.21	0.70 ± 0.19	0.308
Unaided VA, OS	0.67 ± 0.18	0.71 ± 0.19	0.386
BCVA, OD	0.98 ± 0.10	0.99 ± 0.09	0.494
BCVA, OS	0.98 ± 0.11	0.99 ± 0.08	0.516
IOP, OD (mmHg)	16.89 ± 2.04	16.58 ± 1.94	0.581
IOP, OS (mmHg)	16.84 ± 1.72	16.48 ± 1.82	0.497

Blood pressure

Systolic and diastolic blood pressures were reported to be lower in the vitamin D-deficient group ($p = 0.008$ and $p = 0.047$, respectively). Group means and effect estimates were not available in the source manuscript; therefore, the magnitude and clinical relevance of these differences cannot be assessed from the presented data.

IV. Discussion

In this hospital-based cohort of adults with DED, only 9.3% were vitamin D deficient. Schirmer I values were similar in vitamin D-deficient and non-deficient participants in both eyes. No significant between-group differences were observed in visual acuity or IOP. These findings do not support an association between vitamin D deficiency and aqueous tear production as measured by the Schirmer I test in this sample.

Published evidence is inconsistent. Several observational studies from Korea, India, and other populations have reported lower serum 25(OH)D levels or poorer dry-eye parameters among vitamin D-deficient participants [4-7]. Meta-analyses have also reported lower vitamin D levels and worse symptom or tear-production measures in DED, although heterogeneity has been high [10,11]. Conversely, large population-based studies by Jee et al. and Jeon et al. did not identify statistically significant associations between serum vitamin D levels and DED [8,9]. Differences in participant selection, vitamin D thresholds, DED definitions, sunlight exposure, comorbidities, and the tests used to characterize DED may explain these conflicting findings. Interventional studies have reported improvement in tear-film or symptom measures after vitamin D supplementation in deficient patients [12,13], but these treatment-response findings do not establish a baseline causal association between serum vitamin D status and DED.

The present study may have had limited ability to detect modest associations because only 13 participants were vitamin D deficient. A non-significant p-value should not be interpreted as proof that the groups are equivalent. In addition, Schirmer I testing primarily assesses aqueous tear production and does not characterize tear-film stability, ocular-surface staining, osmolarity, meibomian gland function, or symptom burden. Vitamin D may relate more strongly to inflammatory or evaporative components of DED than to Schirmer I values alone.

The blood-pressure differences were secondary findings and were reported without group means, confidence intervals, or adjustment for potential confounders. They should therefore be regarded as exploratory and interpreted cautiously; they do not alter the primary ocular-surface finding.

Strengths of the study include standardized clinical testing, objective serum 25(OH)D measurement, and region-specific data from Northeast India. Limitations include the cross-sectional design, small vitamin D-deficient subgroup, absence of a non-DED control group, reliance on Schirmer I testing without a validated symptom questionnaire or additional tear-film tests, and lack of inflammatory biomarkers. Future studies should include larger and more balanced vitamin D strata, prespecified confounder adjustment, and a comprehensive DED assessment incorporating symptom scores, tear breakup time, ocular-surface staining, osmolarity, and meibomian gland evaluation.

V. Conclusion

Vitamin D deficiency was uncommon in this tertiary-centre cohort from Northeast India and was not associated with lower Schirmer I values. Visual acuity and IOP were also comparable between vitamin D groups. Interpretation is limited by the small deficient subgroup and the use of Schirmer I testing as the principal dry-eye measure. Larger, adequately powered studies using multidimensional DED assessment are required before firm clinical conclusions can be drawn.

Summary

What was known

Vitamin D has been investigated in relation to ocular-surface inflammation and DED, but observational studies and meta-analyses have produced inconsistent findings.

What this study adds

Among 140 adults with DED, vitamin D deficiency was uncommon and was not associated with reduced Schirmer I values. The study provides regional data from Northeast India while highlighting the need for broader dry-eye phenotyping and larger vitamin D-deficient samples.

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Declarations

Patient consent

Written informed consent was obtained from all participants before enrolment.

Ethics approval

The study was approved by the Institutional Ethics Committee of the Regional Institute of Medical Sciences (RIMS), Imphal, Manipur, and was conducted in accordance with the Declaration of Helsinki.

Financial support and sponsorship

Nil.

Conflicts of interest

The authors declare no conflicts of interest.

Data availability statement

De-identified participant data supporting the findings are available from the corresponding author upon reasonable request, subject to institutional and ethical requirements.

Author contributions

Dr. Thejavituo Kire (TK): Study conception and design, patient recruitment, data collection, and initial manuscript drafting.

Dr. Akshay Thakur (AT): Data analysis and interpretation, manuscript revision, preparation of the final submission, and corresponding-author responsibilities.

Dr. Preetika Singh (PS): Critical manuscript review, scientific input, and final manuscript review and approval.