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THE EFFECT OF VITAMIN D3 SUPPLEMENTATION IN CONTROL OF DRY EYE IN INDOOR & OUTDOOR ENVIRONMENT

Original Article

Hamna Ahmad[1]*, Sarmad Siddique[2], Ubaidullah Jan[3], Sobia yousif[1], Iqra Manzoor[1]
[1]Department of Allied Health Sciences, Superior university, Lahore
[2]Department of Emerging Allied Health Technology, Superior university, Lahore
[3]Department of Optometry and Vision Sciences, Superior university, Lahore

Corresponding Author: Hamna Ahmad, hamnabalouch00@gmail.com, Department of Allied Health science, Superior university, Lahore

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ABSTRACT

Background: Dry eye syndrome (DES) is a multifactorial disorder characterized by tear film instability, ocular surface inflammation, and discomfort, often exacerbated by both intrinsic and extrinsic factors. Vitamin D has been recognized for its anti-inflammatory and immunomodulatory properties, with recent studies suggesting a potential link between vitamin D deficiency and DES. However, the impact of vitamin D supplementation on DES parameters remains unclear. This study aimed to evaluate the association between serum 25-hydroxyvitamin D [25(OH)D] levels and DES incidence and to assess the effect of vitamin D3 supplementation on tear film stability and ocular surface health.

Objective: To determine the relationship between serum 25(OH)D levels and DES parameters and to evaluate the therapeutic impact of vitamin D supplementation on tear stability, inflammation, and symptom severity in individuals from indoor and outdoor environments.

Methods: A randomized controlled trial was conducted on 84 individuals diagnosed with DES, including 44 from an indoor environment and 40 from an outdoor environment. Serum 25(OH)D levels were assessed, and DES parameters, including tear film breakup time (TBUT), fluorescein staining score (FSS), eyelid margin hyperemia, conjunctivochalasis (CCH), Schirmer tear secretion test, ocular surface disease index (OSDI) scores, visual analogue scale (VAS) scores, symptom severity, and duration, were evaluated. Participants with vitamin D deficiency received oral supplementation (60,000 IU/week for eight weeks), and follow-up assessments were performed at 2, 4, 6, and 10 weeks.

Results: Serum 25(OH)D levels were significantly lower in DES patients compared to controls, with a mean value of 10.52 ± 4.61 ng/mL. TBUT values improved significantly from 3.910 ± 0.054 to 4.238 ± 0.022 seconds in the indoor group and from 3.680 ± 0.026 to 4.403 ± 0.118 seconds in the outdoor group at the tenth week ($p<0.05$). FSS decreased from 0.880 ± 0.042 to 0.183 ± 0.022 in the indoor group and from 0.685 ± 0.045 to 0.166 ± 0.224 in the outdoor group ($p<0.05$). Hyperemia of the eyelid margin reduced significantly, from 2.582 ± 0.050 to 1.156 ± 0.022 in the indoor group and from 2.270 ± 0.025 to 1.560 ± 0.326 in the outdoor group ($p<0.05$). Schirmer test values increased from 7.053 ± 0.037 mm to 5.821 ± 0.022 mm in the indoor group and from 6.934 ± 0.055 mm to 7.847 ± 0.681 mm in the outdoor group ($p<0.05$). OSDI scores significantly improved from 58.977 ± 4.240 to 10.298 ± 0.028 in the indoor group and from 53.892 ± 4.001 to 0.152 ± 0.165 in the outdoor group ($p<0.05$).

Conclusion: A significant association was observed between serum 25(OH)D levels and DES severity. Vitamin D deficiency was linked to reduced TBUT, tear secretion, and increased ocular surface inflammation. Vitamin D supplementation improved tear film stability, enhanced tear secretion, and alleviated symptoms, suggesting its potential role in DES management. The immunomodulatory effects of vitamin D may influence DES pathogenesis, warranting further research to establish optimal supplementation protocols.

Keywords: Conjunctivochalasis, dry eye syndrome, hyperemia, immunomodulation, ocular surface, Schirmer test, vitamin D

INTRODUCTION

Dry eye syndrome is a multifactorial disorder characterized by discomfort, visual disturbances, and instability of the tear film, often leading to inflammation and potential damage to the ocular surface. The condition is associated with excessive tear evaporation and an increase in tear film osmolarity, resulting in symptoms such as dryness, grittiness, burning sensation, redness, eyelid adhesions upon waking, and transient blurred vision that improves with blinking. Various intrinsic factors, including reduced blink rate, wide lid aperture, aging, hormonal changes, and systemic medications like antihistamines and beta-blockers, contribute to the disease. Additionally, extrinsic environmental factors, such as low humidity, high wind velocity, and occupational exposure, play a crucial role in exacerbating dry eye symptoms. The underlying pathophysiology of dry eye involves disruption of the tear film's stability due to meibomian gland dysfunction, poor lid congruity, and systemic or topical medications that increase tear evaporation. Furthermore, conditions such as vitamin A deficiency, ocular allergies, and contact lens use can compromise the ocular surface and worsen the disease process(1, 2). Recent research has highlighted the potential role of vitamin D in ocular health due to its anti-inflammatory and immunomodulatory properties. Vitamin D exists in two primary forms: ergocalciferol (vitamin D2), derived from plant sources, and cholecalciferol (vitamin D3), synthesized in the skin upon exposure to ultraviolet radiation. Epidemiological studies suggest that vitamin D deficiency is widespread, affecting up to 90% of certain populations, despite adequate sunlight exposure. Vitamin D has been implicated in various ocular conditions, including age-related macular degeneration (ARMD), diabetic retinopathy, and uveitis. Some studies have reported an inverse relationship between serum vitamin D levels and early ARMD, although its association with advanced disease remains unclear. Additionally, vitamin D's role in dry eye syndrome has been explored, with findings indicating that its deficiency may exacerbate symptoms by impairing corneal epithelial barrier function and tear film stability. Evidence suggests that vitamin D promotes epithelial wound healing and reduces ocular inflammation, with Schirmer's test scores and tear breakup time (TBUT) being notably lower in individuals with vitamin D deficiency(3, 4).

Although the link between vitamin D and dry eye syndrome remains debated, some studies have shown that higher serum vitamin D levels correlate with reduced dry eye symptoms, as assessed through subjective patient-reported questionnaires. Vitamin D has also been found to modulate tight junction proteins, such as occludin and ZO-1, which are critical for maintaining corneal epithelial integrity. In animal models, vitamin D supplementation has demonstrated protective effects against ocular surface inflammation, suggesting its potential therapeutic benefit in dry eye disease. In patients with Sjögren's syndrome, a systemic autoimmune condition associated with severe aqueous deficiency, lower vitamin D levels have been documented, reinforcing the hypothesis that vitamin D may play a role in maintaining tear film homeostasis. Given the high prevalence of vitamin D deficiency worldwide and its potential implications for ocular surface health, investigating its role in dry eye disease is essential(5, 6). Despite India's geographical advantage of abundant sunlight, vitamin D deficiency is alarmingly prevalent, raising concerns about its impact on systemic and ocular health. Vitamin D deficiency has been implicated in numerous chronic conditions, including autoimmune diseases, cardiovascular disorders, and metabolic syndromes. Biochemical markers such as 25-hydroxyvitamin D [25(OH)D] serve as reliable indicators of vitamin D status, with levels below 20 ng/mL classified as deficient, leading to disruptions in calcium metabolism and immune regulation. Current recommendations suggest an intake of 200–800 IU of vitamin D daily, depending on age, while short-term high-dose supplementation (60,000 IU per week for eight weeks) is commonly prescribed for deficiency correction(7, 8). Considering the potential role of vitamin D in mitigating dry eye symptoms, this study aims to evaluate the association between serum 25(OH)D levels and the incidence of dry eye syndrome. Additionally, it seeks to assess the impact of vitamin D3 supplementation on clinical outcomes, providing insight into whether vitamin D repletion can serve as an adjunctive therapeutic strategy for managing dry eye disease.

METHODS

A randomized controlled trial was conducted at the Department of Ophthalmology, Superior University, Lahore, to evaluate the effect of vitamin D3 supplementation on dry eye syndrome (DES). The study included 84 participants diagnosed with DES, categorized into two environmental groups: 44 individuals with predominant indoor exposure (spending ≥80% of their daily time indoors) and 40 individuals with significant outdoor exposure (spending ≥80% of their daily time outdoors). Participants were randomly assigned to either the treatment group, which received vitamin D3 supplementation, or the control group, which did not receive supplementation. Randomization was performed using a computer-generated random sequence to ensure unbiased allocation. The primary objective was to assess the association between serum 25-hydroxyvitamin D [25(OH)D] levels and DES parameters, along with evaluating the impact of vitamin D3 supplementation on ocular surface health(9). Serum 25(OH)D levels were measured as the primary biomarker for vitamin D status. DES severity was assessed through standardized clinical evaluations, including tear film breakup time (TBUT), fluorescein staining score (FSS), eyelid margin hyperemia, conjunctivochalasis (CCH), Schirmer tear secretion test, ocular surface disease index (OSDI) scores, visual analogue scale (VAS) for symptom severity, and duration of symptoms. Participants with vitamin D deficiency (serum 25(OH)D <20 ng/mL) in the treatment group received oral vitamin D3 supplementation at a dose of 60,000 IU per week for eight weeks. The control group did not receive vitamin D3 supplementation but was monitored under standard ophthalmic care. Follow-up evaluations of DES parameters were conducted at 2, 4, 6, and 10 weeks to compare pre-treatment and post-treatment changes(10).

Participants were selected based on predefined inclusion and exclusion criteria. Eligible participants were adults aged 18 years and older who met the diagnostic criteria for DES and provided written informed consent. Only individuals without significant systemic illnesses that could affect ocular health were included. Exclusion criteria comprised individuals unable to cooperate with the study procedures, those diagnosed with autoimmune diseases such as Sjögren's syndrome, rheumatoid arthritis, systemic lupus erythematosus, or other immune-mediated disorders. Participants with a history of severe systemic illnesses, including cancer, hematological diseases, or hyperthyroidism, were also excluded. Pregnant or breastfeeding women were not considered. Additionally, individuals with a history of ocular surgery in the past six months, recent use of ophthalmic medications or contact lenses within the last month, or any ocular pathology such as glaucoma, uveitis, retinal hemorrhage, optic neuritis, eyelid abnormalities, or nasolacrimal apparatus dysfunction were excluded from participation(11). Ethical approval was obtained from the Institutional Review Board (IRB) of Superior University, Lahore. Written informed consent was secured from all participants before enrollment, ensuring compliance with ethical guidelines outlined in the Declaration of Helsinki. Confidentiality was maintained, and participants were informed of their right to withdraw from the study at any stage without consequences(12, 13).

Data collection involved standardized ophthalmic assessments and biochemical analyses. TBUT was measured using fluorescein dye, with values less than 10 seconds indicating tear film instability. FSS was graded based on corneal staining severity. Schirmer's test was performed without anesthesia, with tear secretion values below 5 mm indicating severe aqueous deficiency. Subjective symptom severity was recorded using the OSDI and VAS. Serum 25(OH)D levels were quantified using enzyme-linked immunosorbent assay (ELISA)(14, 15). Statistical analysis was conducted using SPSS (version 22). Baseline characteristics were compared between groups using independent t-tests for continuous variables and chi-square tests for categorical variables. Longitudinal changes in DES parameters between pre-treatment and post-treatment evaluations were analyzed using paired t-tests or Wilcoxon signed-rank tests based on data normality. Correlations between serum 25(OH)D levels and DES severity were assessed using Pearson's or Spearman's correlation coefficients. A p-value of <0.05 was considered statistically significant(16). The study methodology was designed to ensure rigorous data collection, methodological transparency, and adherence to ethical research standards. By addressing the potential role of vitamin D3 supplementation in managing DES, the findings aim to provide clinically relevant insights into the relationship between vitamin D status and ocular surface health(17).

Less than Age 50	200 IU
50	400 IU
50-70	600 IU
70+	800 IU

RESULTS

A total of 84 participants diagnosed with dry eye syndrome were included in the study, comprising 44 individuals from an indoor environment and 40 from an outdoor environment. All participants were evaluated for serum 25-hydroxyvitamin D [25(OH)D] levels and underwent repeated follow-up assessments for up to ten weeks after vitamin D3 supplementation. The tear film breakup time (TBUT) values significantly improved in both indoor and outdoor groups over time. Pre-treatment TBUT values were 3.910 ± 0.054 seconds for the indoor group and 3.680 ± 0.026 seconds for the outdoor group. Following supplementation, significant improvements were observed at each follow-up, with the highest TBUT values recorded at the tenth week, reaching 4.238 ± 0.022 seconds in the indoor group and 4.403 ± 0.118 seconds in the outdoor group. The fluorescein staining score (FSS) demonstrated a significant reduction in both groups, particularly up to the sixth week. In the indoor group, FSS declined from 0.880 ± 0.042 at baseline to 0.183 ± 0.022 at the tenth week, while in the outdoor group, the decrease was from 0.685 ± 0.045 to 0.166 ± 0.224. The most substantial differences were observed in the initial weeks, with significance levels diminishing by the tenth week. Hyperemia of the eyelid margin showed a highly significant decrease across follow-ups, reflecting a positive response to vitamin D supplementation. The pre-treatment hyperemia grade in the indoor group was 2.582 ± 0.050, which reduced to 1.156 ± 0.022 at the tenth week, while in the outdoor group, it declined from 2.270 ± 0.025 to 1.560 ± 0.326.

The values for conjunctivochalasis (CCH) significantly differed after the second and fourth weeks of vitamin D supplementation but did not show statistically significant changes at the sixth and tenth weeks. In the indoor group, the CCH grade decreased from 0.679 ± 0.041 at baseline to 0.073 ± 0.026 at the tenth week, while in the outdoor group, the reduction was from 0.622 ± 0.043 to 0.132 ± 0.173. The Schirmer tear secretion test values improved significantly in both groups, indicating an increase in tear production. In the indoor group, baseline values were 7.053 ± 0.037 mm, which improved to 5.821 ± 0.022 mm at the tenth week. The outdoor group exhibited a more pronounced improvement, with values increasing from 6.934 ± 0.055 mm to 7.847 ± 0.681 mm, suggesting that vitamin D supplementation alleviated dry eye symptoms by enhancing tear secretion. The ocular surface disease index (OSDI) scores significantly improved over time. In the indoor group, pre-treatment OSDI scores were 58.977 ± 4.240, which decreased to 10.298 ± 0.028 at the tenth week. Similarly, the outdoor group demonstrated a decline from 53.892 ± 4.001 to 0.152 ± 0.165. The visual analogue scale (VAS) values decreased more prominently in the indoor group compared to the outdoor group, with pre-treatment scores of 3.194 ± 0.050 in

the indoor group and 3.152 ± 0.030 in the outdoor group. By the tenth week, the VAS score in the indoor group had reduced to 0.580 ± 0.029, while in the outdoor group, it reached 0.946 ± 0.374, indicating a greater improvement in symptom perception among indoor individuals.

The severity of symptoms and duration of symptoms significantly differed between groups throughout the study period. In the indoor group, the severity of symptoms grade declined from 2.407 ± 0.036 to 1.137 ± 0.031 at the tenth week, while in the outdoor group, the reduction was from 3.141 ± 0.033 to 1.275 ± 0.298. Similarly, the duration of symptoms grade improved from 2.310 ± 0.053 at baseline to 1.428 ± 0.027 in the indoor group and from 3.167 ± 0.045 to 1.147 ± 0.289 in the outdoor group. In the female subgroup, consisting of 54 individuals, TBUT values significantly improved in both indoor and outdoor environments up to the sixth week, but the differences were non-significant at the tenth week. Pre-treatment TBUT values were 3.287 ± 0.028 seconds in the indoor group and 3.194 ± 0.033 seconds in the outdoor group. The highest values were recorded at the sixth week, with 5.094 ± 0.068 seconds in the indoor group and 4.935 ± 0.035 seconds in the outdoor group. However, by the tenth week, TBUT values in both groups showed no further significant changes, indicating that the effect of vitamin D supplementation on TBUT might stabilize over time.

Fluorescein staining scores in females were not significantly different before and after treatment up to the fourth week but showed a significant improvement at the sixth week. In the indoor group, FSS values declined from 0.672 ± 0.045 at baseline to 0.146 ± 0.201 at the tenth week, while in the outdoor group, the reduction was from 0.586 ± 0.039 to 0.118 ± 0.020. Hyperemia of the eyelid margin showed non-significant differences up to the fourth week but became highly significant at the sixth and tenth weeks. In the indoor group, pre-treatment values were 2.550 ± 0.040, which reduced to 1.515 ± 0.295 at the tenth week. Similarly, in the outdoor group, values decreased from 2.457 ± 0.032 to 0.998 ± 0.064. Schirmer tear secretion test values significantly improved in both groups, indicating enhanced tear production following vitamin D supplementation. The indoor group showed an improvement from 8.559 ± 0.049 mm at baseline to 8.934 ± 0.969 mm at the tenth week, while in the outdoor group, values improved from 8.476 ± 0.038 mm to 7.690 ± 0.032 mm. OSDI scores showed a significant improvement in both groups, reflecting enhanced ocular health and reduced dry eye symptoms. In the indoor group, OSDI scores declined from 37.296 ± 3.750 at baseline to 20.995 ± 1.487 at the tenth week. Similarly, in the outdoor group, values decreased from 34.074 ± 3.529 to 19.398 ± 0.022.

VAS scores differed highly significantly at the second and tenth weeks after vitamin D supplementation but showed non-significant differences at the fourth and sixth weeks. In the indoor group, the VAS score declined from 3.370 ± 1.445 at baseline to 1.494 ± 0.283 at the tenth week, while in the outdoor group, values reduced from 3.111 ± 0.974 to 1.247 ± 0.025. The severity of symptoms and duration of symptoms grades also showed highly significant reductions over time. In the indoor group, severity scores decreased from 2.245 ± 0.031 to 1.354 ± 0.239 at the tenth week, while in the outdoor group, values reduced from 2.196 ± 0.031 to 1.163 ± 0.020. Similarly, the duration of symptoms grade improved from 2.330 ± 0.056 to 1.262 ± 0.053 in the indoor group and from 2.245 ± 0.031 to 1.116 ± 0.016 in the outdoor group. The findings suggest that vitamin D supplementation significantly improved multiple DES parameters in both indoor and outdoor environments. While some improvements were more pronounced in the initial weeks, the sustained benefits on tear film stability, ocular inflammation, and subjective symptom relief were evident up to the tenth week.

Table: Comparison between indoor and outdoor regarding the values of Dry eye syndrome parameters before and after vitamin D supplementation for male respondents.

			After vitamin D inclusion							
Indoor: Outdoor (N)		Pre-treatment	W_2		W_4		W_6		W_{10}	
		44:40	32:27		30:27		32:27		30:27	
		Mean ± SD	Mean ± SD	P-value	Mean ± SD	P-value	Mean ± SD	P-value	Mean ± SD	P-value
TBUT (sec)	Indoor	3.910 ± 0.054	5.709±0.328	0.001	4.913±0.068	0.000	4.538±0.030	0.000	4.238±0.022	0.000
	Outdoor	3.680 ± 0.026	5.473±0.147		5.277±0.331		5.195±0.397		4.403±0.118	
FSS (grade)	Indoor	0.880 ± 0.042	0.289±0.013	0.000	0.253±0.159	0.027	0.203±0.015	0.022	0.183±0.022	0.680
	Outdoor	0.685 ± 0.045	0.434±0.113		0.358±0.189		0.294±0.217		0.166±0.224	
Hyperemia of eyelid margin (grade)	Indoor	2.582 ± 0.050	1.284±0.068	0.008	1.247±0.143	0.011	1.212±0.024	0.002	1.156±0.022	0.000
	Outdoor	2.270 ± 0.025	1.178±0.206		1.126±0.200		1.036±0.304		1.560±0.326	
CCH (grade)	Indoor	0.679 ± 0.041	0.310±0.024	0.025	0.241±0.102	0.123	0.194±0.029	0.202	0.073±0.026	0.068
	Outdoor	0.622 ± 0.043	0.378±0.167		0.305±0.197		0.240±0.196		0.132±0.173	
Schirmer tear secretion test (mm)	Indoor	7.053 ± 0.037	6.947±0.148	0.000	6.577±0.047	0.000	6.343±0.016	0.000	5.821±0.022	0.000
	Outdoor	6.934 ± 0.055	8.766±0.407		8.616±0.457		8.493±0.238		7.847±0.681	
OSDI score	Indoor	58.977±4.240	22.328±0.165	0.000	19.801±0.835	0.000	14.665±0.077	0.000	10.298±0.028	0.000
	Outdoor	53.892±4.001	19.392±0.560		12.343±0.213		7.211±0.271		0.152±0.165	
VAS score	Indoor	3.194 ± 0.050	1.269±0.047	0.000	1.162±0.116	0.000	0.827±0.028	0.000	0.580±0.029	0.000
	Outdoor	3.152 ± 0.030	3.045±0.478		2.782±0.524		1.676±0.233		0.946±0.374	

Severity of symptoms (grade)	Indoor	2.407 ± 0.036	2.500 ± 0.359	0.000	2.080±0.035	0.000	1.926±0.022	0.000	1.137±0.031	0.014
	Outdoor	3.141 ± 0.033	1.706 ± 0.188		1.613±0.260		1.504±0.266		1.275±0.298	
Duration of symptoms (grade)	Indoor	2.310 ± 0.053	1.747 ±0.051	0.000	1.241±0.014	0.000	0.874±0.026	0.000	1.428±0.027	0.000
	Outdoor	3.167 ± 0.045	1.519±0.240		1.419±0.254		1.289±0.243		1.147±0.289	

NS = Non-significant (P>0.05); * = Significant (P<0.05); ** = Highly significant (P<0.01)

SD = Standard deviation

TBUT=tear break-up time; FSS=fluorescein staining score; CCH=conjunctivochalasis; OSDI=ocular surface disease index; VAS=visual analogue scale

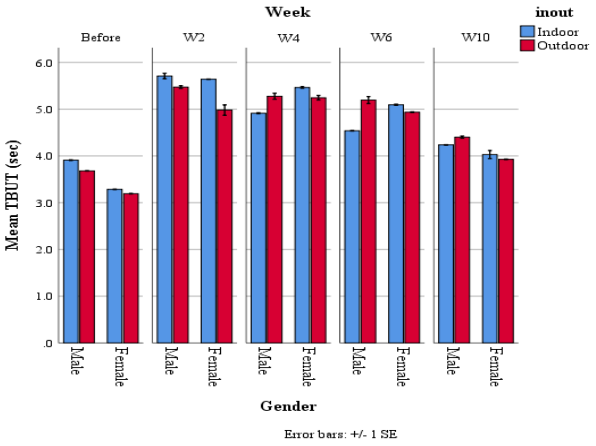
Table: Comparison between indoor and outdoor regarding the values of Dry eye syndrome parameters before and after vitamin D supplementation female respondents.

Indoor: Outdoor (N)			**After vitamin D inclusion**							
		Pre-treatment	W_2		W_4		W_6		W_{10}	
		27:27	22:16		22:16		22:16		22:16	
		Mean ± SD	Mean ± SD	P-value	Mean ± SD	P-value	Mean ± SD	P-value	Mean ± SD	P-value
TBUT (sec)	Indoor	3.287±0.028	5.641±0.027	0.000	5.464±0.095	0.000	5.094±0.068	0.000	4.030±0.475	0.394
	Outdoor	3.194±0.033	4.981±0.446		5.245±0.196		4.935±0.035		3.928±0.028	
FSS (grade)	Indoor	0.672±0.045	0.422±0.036	0.122	0.341±0.044	0.111	0.183±0.054	0.003	0.146±0.201	0.589
	Outdoor	0.586±0.039	0.362±0.205		0.294±0.146		0.137±0.033		0.118±0.020	
Hyperemia of eyelid margin (grade)	Indoor	2.550±0.040	1.322±0.044	0.072	1.147±0.035	0.169	1.031±0.056	0.000	1.515±0.295	0.000
	Outdoor	2.457±0.032	1.223±0.291		1.095±0.202		0.926±0.021		0.998±0.064	
CCH (grade)	Indoor	0.942±0.032	0.392±0.036	0.023	0.313±0.037	0.200	0.269±0.041	0.000	0.196±0.218	0.251

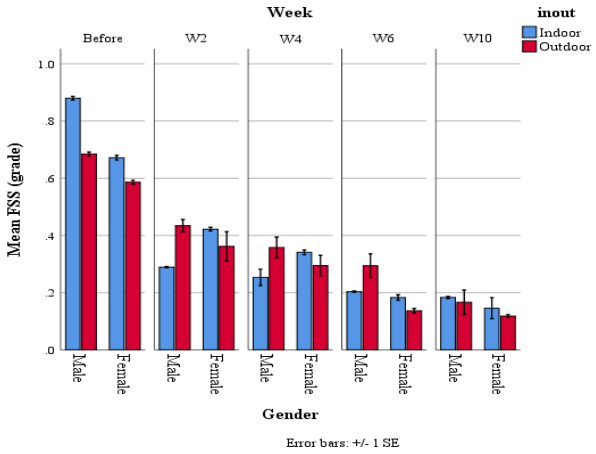
	Outdoor	0.893±0.033	0.314±0.175		0.261±0.216		0.197±0.034		0.132±0.027	
Schirmer tear secretion test (mm)	Indoor	8.559±0.049	8.994±0.159	0.001	9.761±0.167	0.000	9.682±0.234	0.003	8.934±0.969	0.000
	Outdoor	8.476±0.038	7.500±2.366		8.449±0.327		8.688±1.740		7.690±0.032	
OSDI score	Indoor	37.296±3.750	31.720±2.666	0.003	28.275±3.473	0.001	25.818±0.273	0.001	20.995±1.487	0.000
	Outdoor	34.074±3.529	29.188±2.613		25.225±0.351		23.063±4.123		19.398±0.022	
VAS score	Indoor	3.370±1.445	2.443±0.056	0.004	2.236±0.575	0.440	2.133±0.409	0.086	1.494±0.283	0.001
	Outdoor	3.111±0.974	2.241±0.357		2.116±0.282		1.951±0.045		1.247±0.025	
Severity of symptoms (grade)	Indoor	2.245±0.031	1.681±0.045	0.000	1.589±0.041	0.000	1.427±0.286	0.000	1.354±0.239	0.003
	Outdoor	2.196±0.031	1.490±0.182		1.418±0.189		1.128±0.025		1.163±0.020	
Duration of symptoms (grade)	Indoor	2.330±0.056	1.492±0.037	0.001	1.578±0.038	0.000	1.358±0.251	0.002	1.262±0.053	0.000
	Outdoor	2.245±0.031	1.349±0.206		1.360±0.169		1.149±0.026		1.116±0.016	

NS = Non-significant (P>0.05); * = Significant (P<0.05); ** = Highly significant (P<0.01) SD = Standard deviation

TBUT=tear break-up time; FSS=fluorescein staining score; CCH=conjunctivochalasis; OSDI=ocular surface disease index; VAS=visual analogue scale



The effects of vitamin D supplementation on dry eye syndrome in the indoor and outdoor environment (A)



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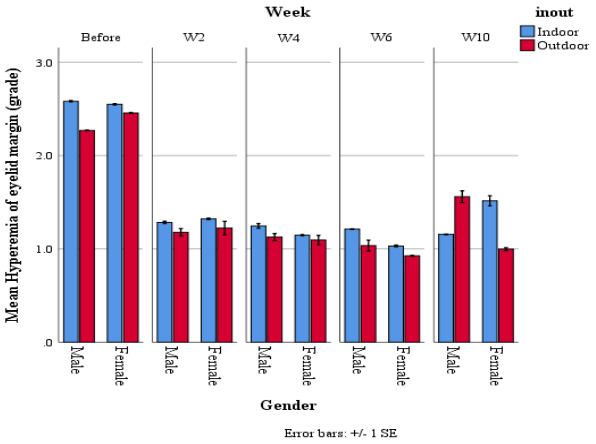
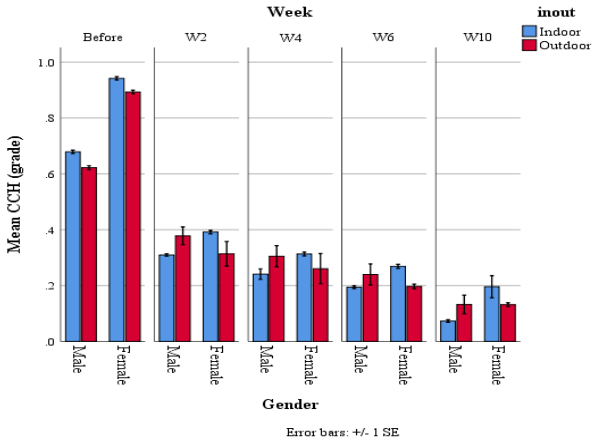
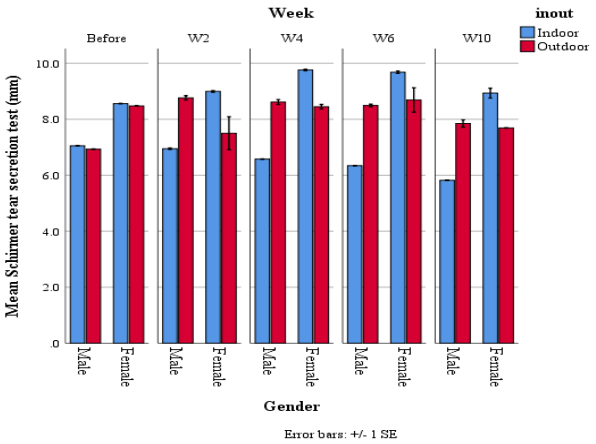


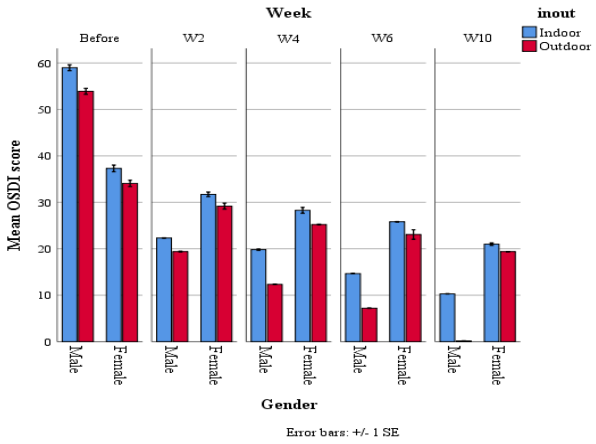
The effects of vitamin D supplementation on dry eye syndrome in the indoor and outdoor environment (C)



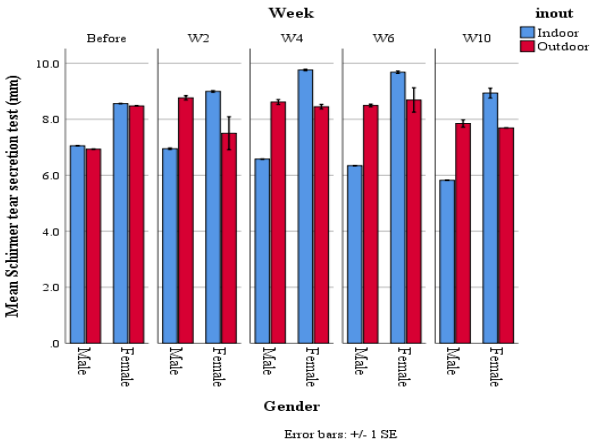
The effects of vitamin D supplementation on dry eye syndrome in the indoor and outdoor environment (D)



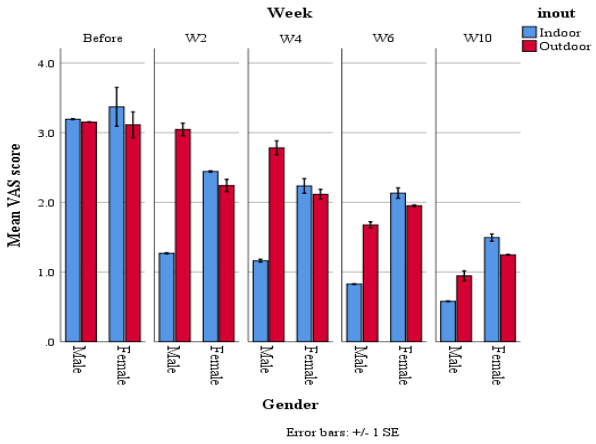
The effects of vitamin D supplementation on dry eye syndrome in the indoor and outdoor environment (E)



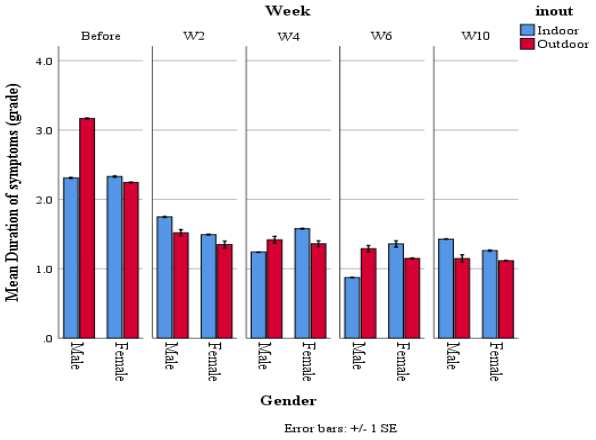
The effects of vitamin D supplementation on dry eye syndrome in the indoor and outdoor environment (F)



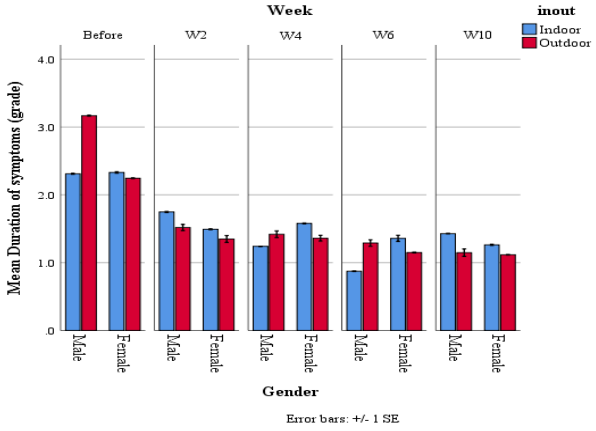
The effects of vitamin D supplementation on dry eye syndrome in the indoor and outdoor environment (G)



The effects of vitamin D supplementation on dry eye syndrome in the indoor and outdoor environment (H)



The effects of vitamin D supplementation on dry eye syndrome in the indoor and outdoor environment (I)



The effects of vitamin D supplementation on dry eye syndrome in the indoor and outdoor environment (J)

DISCUSSION

The findings of this study reinforce the growing evidence linking dry eye syndrome (DES) with vitamin D deficiency. The results demonstrated a significant improvement in various DES parameters, including tear film breakup time (TBUT), fluorescein staining score (FSS), hyperemia of the eyelid margin, tear secretion, and subjective symptom scores following vitamin D supplementation. These findings align with previous research suggesting that vitamin D plays a crucial role in tear film stability, ocular surface integrity, and inflammatory modulation. The improvement in TBUT following supplementation underscores the role of vitamin D in reducing tear film instability, which is known to be one of the primary mechanisms driving DES. Tear hyperosmolarity and instability trigger ocular surface damage and inflammatory cascades, perpetuating the disease process. The observed increase in TBUT values after supplementation supports the hypothesis that vitamin D has protective effects on tear film dynamics, likely through its anti-inflammatory and immunomodulatory properties(18). The reduction in FSS and eyelid margin hyperemia further supports the anti-inflammatory effects of vitamin D on the ocular surface. Fluorescein staining has long been used to assess epithelial damage, while hyperemia of the eyelid margin is associated with meibomian gland dysfunction, a leading cause of evaporative DES. The significant reduction in these parameters after supplementation suggests that vitamin D may enhance epithelial barrier function, promote ocular surface healing, and reduce meibomian gland inflammation. This aligns with previous reports indicating that vitamin D downregulates pro-inflammatory cytokines such as TNF-α and IFN-γ, which are key mediators in DES pathophysiology. The improvement in tear secretion, as evidenced by higher Schirmer test values post-supplementation, suggests that vitamin D may also play a role in promoting lacrimal gland function, further contributing to enhanced ocular hydration(19, 20).

A notable finding in this study was the significant improvement in subjective symptoms, including OSDI scores, visual analogue scale (VAS) scores, and symptom severity and duration following vitamin D supplementation. The correlation between vitamin D levels and symptom relief highlights its potential role in alleviating neuropathic pain associated with DES. Chronic ocular discomfort in DES has

been linked to central pain sensitization, and vitamin D has been shown to modulate neuroinflammatory pathways, reduce hypersensitivity, and improve overall pain perception. The observed improvement in symptom scores suggests that vitamin D may not only improve tear film parameters but also provide symptomatic relief by modulating pain pathways. However, the return of some parameters to near-baseline levels after ten weeks suggests that sustained vitamin D supplementation may be necessary for long-term symptom control(21, 22). This study also highlights differences in the response to vitamin D supplementation based on gender. While TBUT improved in both male and female participants, FSS and tear secretion exhibited more pronounced improvements in females. Previous studies have suggested that vitamin D metabolism differs between males and females due to its interaction with estrogen biosynthesis and signaling. Vitamin D has been reported to have anti-estrogenic activity, which may influence its effects on the ocular surface and tear film stability. The influence of hormonal variations on vitamin D metabolism could explain the differential response observed between genders. Age-related differences in vitamin D synthesis and bioavailability may further contribute to variations in response, as younger individuals demonstrated greater improvement in FSS and tear secretion compared to older participants. These findings indicate that individualized vitamin D supplementation strategies, considering gender and age-related differences, may be necessary to optimize its therapeutic benefits for DES(23, 24).

Despite these promising findings, this study has certain limitations. The study duration was limited to ten weeks, which may not fully capture the long-term effects of vitamin D supplementation on DES. The lack of a placebo-controlled arm limits the ability to determine whether the observed improvements were solely due to vitamin D supplementation or influenced by other factors, such as seasonal variations in sunlight exposure. Additionally, while serum 25-hydroxyvitamin D levels were assessed, direct correlations between these levels and the degree of symptom improvement were not extensively analyzed. Future studies with larger sample sizes, longer follow-up periods, and placebo-controlled designs are necessary to validate these findings and explore optimal dosing regimens for sustained benefits(25). The results suggest that vitamin D supplementation could be an effective adjunctive treatment for DES, particularly in individuals with documented vitamin D deficiency. The observed improvements in tear film stability, ocular inflammation, and symptom relief highlight its potential role in the management of DES. However, given the transient nature of the observed benefits, sustained supplementation protocols should be explored. Future research should also investigate whether combination therapies, such as vitamin D supplementation alongside conventional DES treatments, could provide enhanced therapeutic outcomes. Understanding the underlying mechanisms of vitamin D's effects on tear film homeostasis, inflammation, and ocular pain pathways could pave the way for more targeted treatment approaches in DES management.

CONCLUSION

The findings of this study highlight the significant role of vitamin D supplementation in improving dry eye syndrome by enhancing tear film stability, reducing ocular surface inflammation, and alleviating symptoms. The observed improvements in tear breakup time, ocular surface integrity, tear secretion, and symptom relief suggest that vitamin D may serve as a beneficial adjunct in the management of dry eye disease, particularly in individuals with vitamin D deficiency. The results also indicate potential variations in response based on gender and environmental exposure, emphasizing the need for personalized approaches to supplementation. While the study supports the therapeutic potential of vitamin D in dry eye management, sustained supplementation and further research are necessary to establish long-term efficacy and optimal treatment strategies. These findings contribute to the growing body of evidence linking vitamin D to ocular health and suggest its relevance in improving the quality of life for individuals affected by dry eye syndrome.

Author Contribution

Author	Contribution
Hamna Ahmad	Conceptualization, Methodology, Formal Analysis, Writing - Original Draft, Validation, Supervision
Sarmad Siddique	Methodology, Investigation, Data Curation, Writing - Review & Editing
Ubaidullah Jan	Investigation, Data Curation, Formal Analysis, Software
Sobia Yousif	Software, Validation, Writing - Original Draft
Iqra Manzoor	Formal Analysis, Writing - Review & Editing

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