

# Role of Vitamin D3 Supplementation in the Treatment of Dry Eye Syndrome



Bushra Kanwal<sup>1</sup>, Ayesha Kiran<sup>2</sup>, Muhammad Junaid Iqbal<sup>3</sup>, Iqra Khalil<sup>4</sup>, Aghna Maryam<sup>5</sup>  
<sup>1,2,4</sup> The University of Faisalabad, <sup>3,5</sup>University of Urbino "Carlo Bo", Italy

## ABSTRACT

**Purpose:** The aim of this study was to evaluate the role of vitamin D3 supplementation in treating non-Sjogren dry eye (NSDE) patients compared to the conventional treatment with artificial tears.

**Study Design:** Non-randomized controlled Trial.

**Place and duration of study:** Rural Health Centre (RHC) Buchaal Kalan from September 2021 to July 2022

**Methods:** This study allocated 108 patients with NSDE and hypovitaminosis D via two-arm parallel assignment. The sample was divided into two groups by non-probability purposive sampling. Group 1 received conventional treatment as artificial tears 4 times/day and group 2 was given oral vitamin D3 supplementation of 6000 IU daily along with artificial tears for a period of 90 days. The impact of oral vitamin D3 supplementation on NSDE was assessed by comparing means of ocular parameters of both groups over time. Tear break-up time (TBUT) in seconds and Schirmer's test (ST) score in millimeters were primary outcome measures. The ocular surface disease index (OSDI) score and numerical pain rating scale (NPRS) were secondary outcome measures.

**Results:** The mean age of patients in group 1 and group 2 was 34.98±8.64 and 34.87±8.79 respectively. Similarly, the mean serum 25 (OH) D level was 15.03±3.27 in group 1 and 14.93±3.26 in group 2. Results showed that OSDI and NPRS scores were decreased in both groups, however, TBUT and ST scores were improved in group 2.

**Conclusion:** Oral vitamin D3 supplementation may serve as a new treatment option for NSDE patients having hypovitaminosis D.

**Trial Register Number:** NCT05425914.

**Keywords:** Tears, Non-Sjogren Dry Eye, Anti-Inflammatory, Dry Eye Syndrome, Vitamin D Deficiency.

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Correspondence to: Bushra Kanwal  
The University of Faisalabad  
Email: bushra.kanwal22446688@gmail.com

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## INTRODUCTION

Dry eye disease (DED) is a chronic, multifactorial and highly prevalent ocular condition that is often characterized by disrupted tear film homeostasis.<sup>1</sup> It is caused by abnormalities of tear film layers including

lipid, aqueous, and mucous layers. Hyperosmolarity, instability of tear film, ocular surface inflammatory changes and neurosensory anomalies have contributory roles in the development of this disease.<sup>2</sup> Approximately 5–34% of the world population is affected by DED and it increases with age.<sup>3</sup> It is classified as aqueous deficient dry eye (ADDE) and evaporative dry eye (EDE). ADDE is divided into Sjögren and non-Sjögren dry eye (NSDE). EDE is sub-classified as intrinsic and extrinsic categories.<sup>4</sup> DED results in symptoms of ocular discomfort, dryness, visual disturbance, and irritation.<sup>5</sup>

Vitamin D is a hormone precursor that plays an important role in the metabolism of bones and immunomodulation. It is present in nature as; either ergocalciferol (vitamin D<sub>2</sub>) which is present in few fish species and plants or cholecalciferol (vitamin D<sub>3</sub>) which is synthesized in the skin upon sunlight exposure.<sup>6</sup> Reduced levels of vitamin D<sub>3</sub> are associated with several serious diseases including cardiovascular system (CVS) disorders, tumors, diabetes, tuberculosis (TB), and osteoporosis. Lower levels of vitamin D can cause obesity and may retard bone growth and health in both children and adults.<sup>7</sup> About 50% of the population in the world is suffering from vitamin D insufficiency on the basis of serum 25-hydroxyvitamin D (25 (OH) D) level < 20 ng/ml.<sup>8</sup> In Pakistan, about 60-90 % of women are vitamin D deficient, improper diet and poor socioeconomic status may have a contributory role in it.

Vitamin D has anti-inflammatory and immune-regulatory properties in addition to its role in calcium metabolism.<sup>3</sup> Previous studies have demonstrated a relationship between Sjogren syndrome and vitamin D deficiency. In a study by Kurtul et al, it was shown that vitamin D deficiency lowers the TBUT and Schirmer tests and may be linked to symptoms of dry eyes in non-Sjögren syndrome.<sup>9</sup>

Vitamin D alters tear cytokines thus reducing inflammation and improving ocular signs and symptoms of the disease. It inhibits T-cells activation and production of various mediators of inflammation e.g., several interleukins, tumor necrosis factor alpha (TNF- $\alpha$ ) and C-reactive protein (CRP).<sup>10</sup>

Various ocular structures like the cornea, sclera, ciliary body, and retina contain vitamin D receptors (VDR), which play a vital role in the physiology of the eye.<sup>11</sup> Cornea has the ability to activate and metabolize vitamin D. Inactive vitamin D is converted into an active form by 1 $\alpha$ -hydroxylase or 24-hydroxylase in the anterior segment of the eye. Megalin and Cubilin are found in lacrimal and accessory lacrimal glands, both are responsible for the production of tears.<sup>12</sup> The megalin receptor has its reputation as a scavenger receptor and enables nonspecific protein absorption by cells. Megalin has several ligands, one of which is the vitamin D binding protein (DBP). Another endocytic receptor with the ability to bind DBP is Cubilin, which has been found to co-express with Megalin in a number of absorptive epithelia. Megalin and Cubilin have a role in the lacrimal gland secretory pathway for vitamin D, which excretes vitamin D metabolites into

the lacrimal fluid.<sup>12</sup>

Corneal epithelial cells can produce vitamin D<sub>3</sub> metabolites after ultra-violet B (UVB) exposure in the presence of 7-dehydrocholesterol. Oral vitamin D supplements affect the concentration of these metabolites in the anterior segment,<sup>13</sup> thus promoting tear secretion, reducing ocular surface inflammation and tear film instability.<sup>14</sup> Very little work has been done on impact of vitamin D supplementation on ocular surface parameters. In the present study, we investigated the impact of oral vitamin D<sub>3</sub> supplements on signs and ocular symptoms of NSDE and aimed to suggest a new treatment option for NSDE contrary to conventional treatment with artificial tears.

## METHODS

This non-randomized clinical trial was conducted at Rural Health Centre (RHC) Buchaal Kalan after approval by the ethical institutional review board (TUF/IRB/046/2022). Informed written consent was obtained from participants. Patients with 20 to 50 years of age, either gender and NSDE were included. Complete history including ocular, medical, and family history was taken. Sample size was calculated via online clinical calculator. Data were collected via specially designed proforma and included demographic information and clinical findings. All the patients with symptoms of vitamin D deficiency in the medical outpatient department (OPD) were first sent to eye OPD for dry eye assessment. After ocular examination, blood samples of dry eye patients were sent to a laboratory for assessment of serum level of vitamin D. Patients having serum 25(OH) D level <25 ng/ml along with TBUT <5 seconds and ST score <10 mm in five minutes were selected for examination. Patients suffering from autoimmune diseases (e.g., Sjögren syndrome and lupus syndrome), diabetes, other ocular pathologies, contact lens users, history of ocular surgery, postmenopausal women and other systemic pathologies that affect tear layers were excluded from study.

Ocular signs were investigated by TBUT and ST scores, and symptoms were assessed via ocular surface disease index (OSDI) and numerical pain rating scale (NPRS) scores.

Following investigative procedures were carried out; best corrected visual acuity (BCVA), slit-lamp examination, fundoscopy, TBUT, quantitative tear

assessment via Schirmer strips, NPRS, and OSDI score on days 0, 15, 30, 60 and 90. Assessment of blood serum vitamin D was performed by Cobas e 411, a fully automated electrochemiluminescence immunoassay (ECLIA) based analyzer. Hypovitaminosis D was considered if total vitamin D was <25 ng/mL. A total of 108 patients with lower vitamin D level and NSDE were randomly allocated into two groups, each containing 54

participants as follow:

Group 1: 0.3% hydroxypropyl methylcellulose 4 times/day were prescribed from day 0 to 90 for symptomatic relief.

Group 2: oral vitamin D3 supplementation of 6000 IU daily along with artificial tears was prescribed from day 0 to 90. A previous study found that all adults who are vitamin D deficient can be treated with 50,000 IU

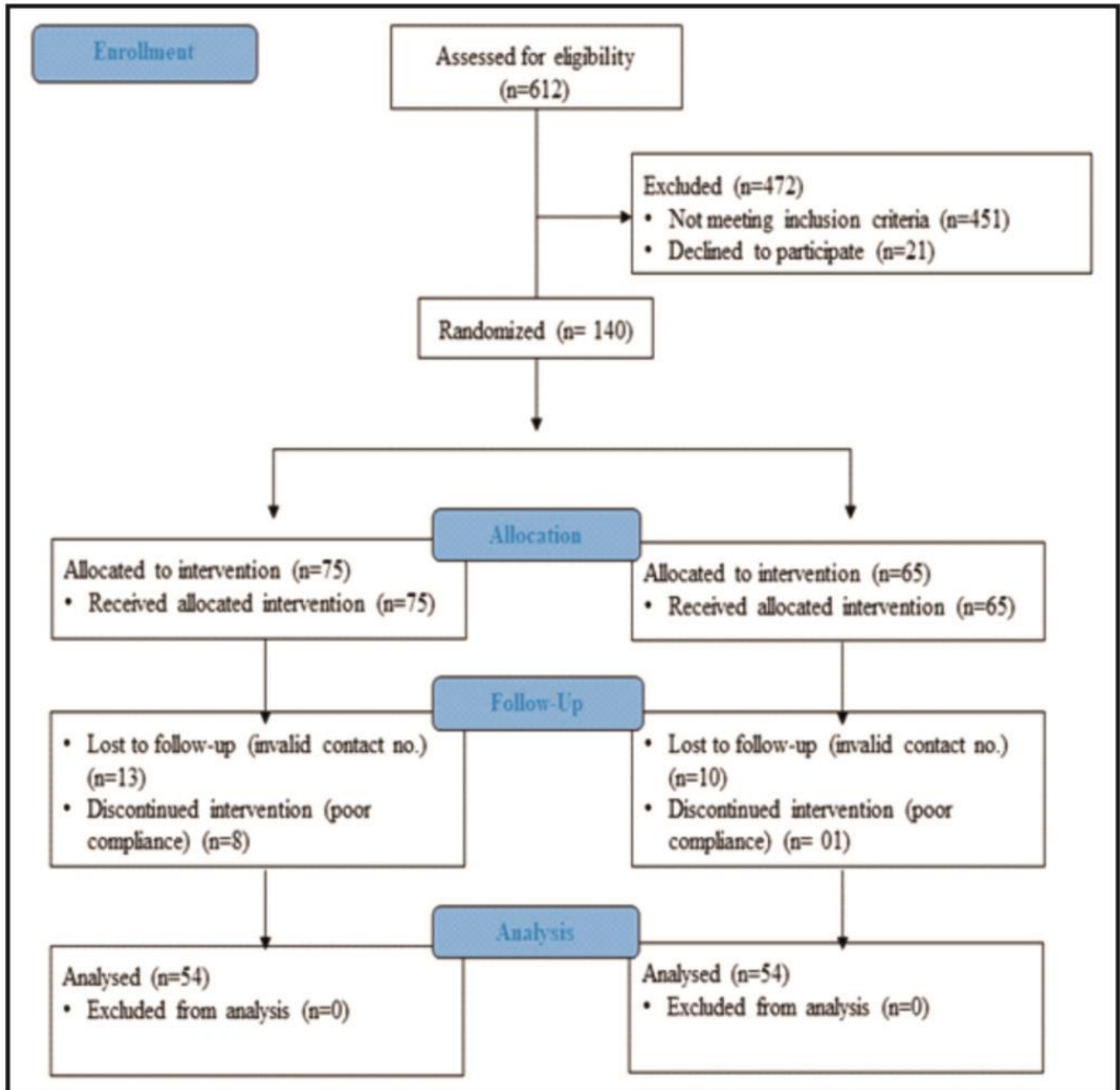


Figure 1: CONSORT diagram depicting participant inclusion, exclusion, and flow during the study.

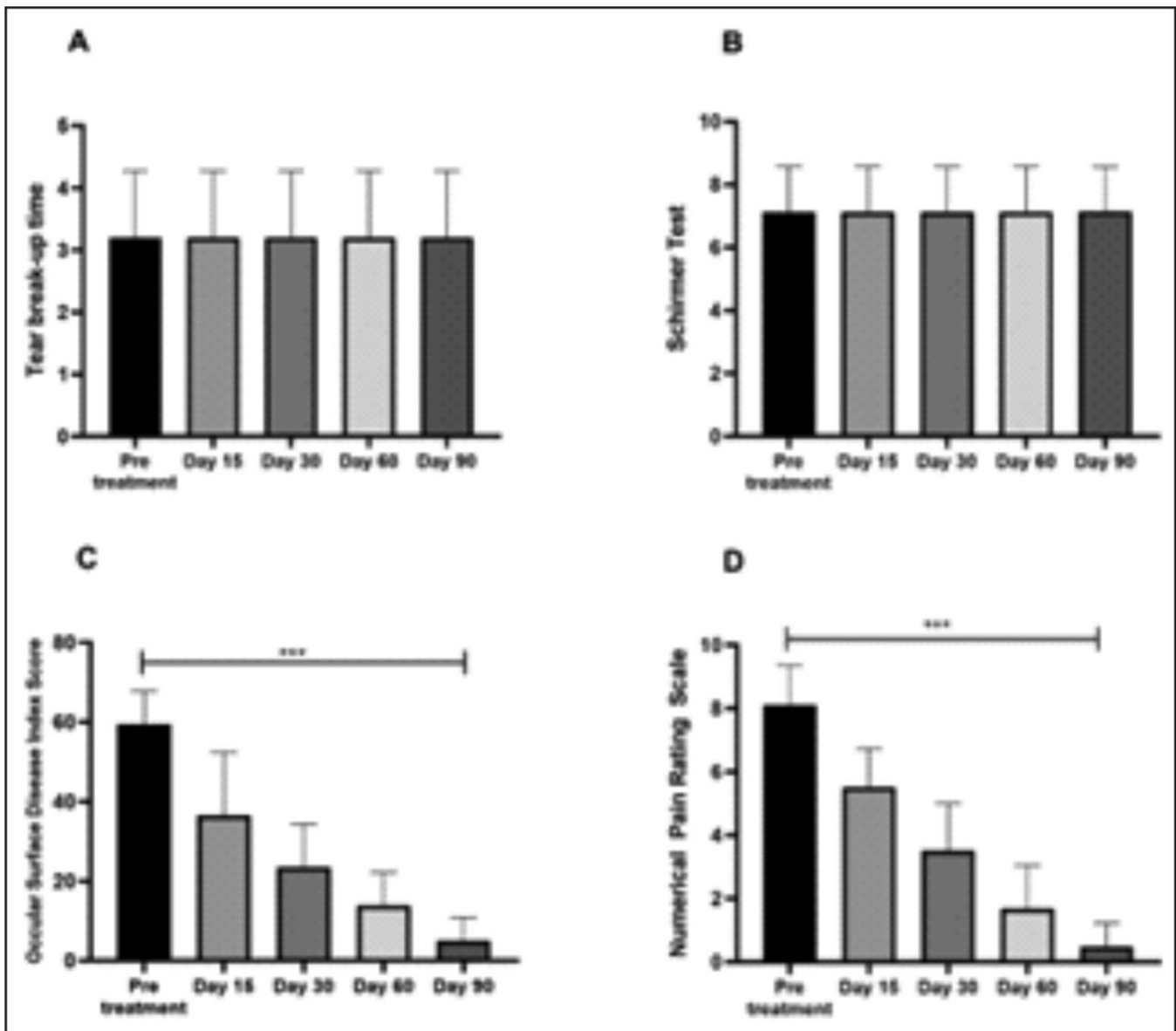
of vitamin D2 or vitamin D3 once a week for 8 weeks, or its equivalent of 6,000 IU of vitamin D2 or vitamin D3 daily to achieve a blood level of 25(OH)D above 30 ng/ml in less time.<sup>15</sup> This study served as the basis for the recommended dose.

Data were presented in the form of mean and standard deviation. Mann-Whitney U test was used to compare both groups over extended period, Friedman test was used for comparison of ocular parameters of individual groups over time. Statistical analysis was done by SPSS version 20 and *P* value less than 0.05 was considered significant.

## RESULTS

A total of 108 subjects were included in this study. Mean age of patients in group 1 and group 2 was 34.98±8.64 and 34.87±8.79 respectively. Similarly, mean serum level was 15.03±3.27 in group 1 and 14.93±3.26 in group 2.

Results showed no significant improvement in TBUT (*p*=0.165) and ST score (*p*=0.406), but OSDI and NPRS scores were significantly decreased (*p*<0.01) on repeated follow-up. Results showed that ocular symptoms were improved with artificial tears in



**Figure 2:** Effects of conventional dry eye treatment (without vitamin D) on non-Sjogren dry eye over time (A) Tear break-up time (TBUT) score was not improved over time (*p*=0.165) (B) Schirmer's test (ST) score was not improved over time (*p*= 0.406) (C) Ocular surface disease index (OSDI) score was significantly improved after treating with artificial tears (*p*<0.01) by Friedman Test (D) Numerical pain rating scale (NPRS) score was significantly improved after treating with artificial tears (*p*<0.01) by Friedman Test.

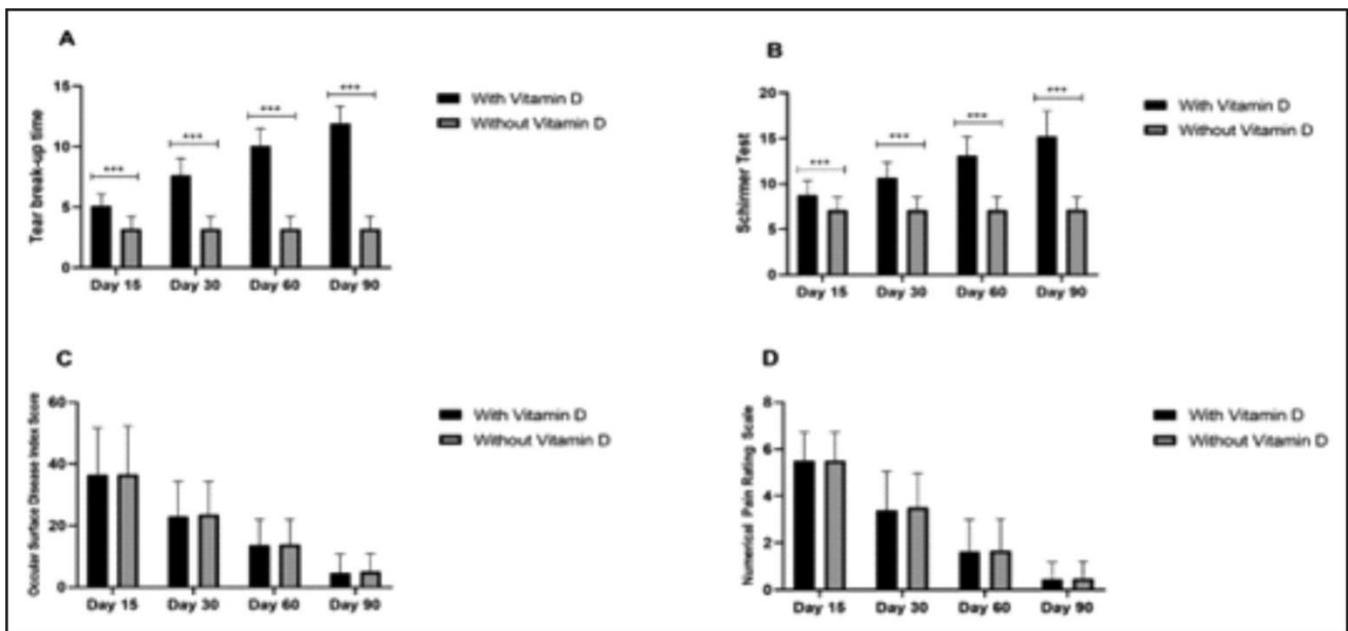
group 1 (Figure 2).

The impact of oral vitamin D3 supplementation on NSDE was evaluated by comparing the ocular parameters of two distinct groups over time (Figure 3). At the baseline, both groups recorded a mean TBUT of  $3.20 \pm 1.06$ . For Group 1 (without vitamin D), these measurements remained consistent. In contrast, Group 2 (receiving vitamin D) demonstrated a consistent ascent in TBUT scores on days 15, 30, 60, and 90 ( $p < 0.01$ ). Specifically, Group 2 TBUT values progressed from the baseline  $3.20 \pm 1.06$  to  $5.11 \pm 0.99$  on day 15, advancing further to  $7.65 \pm 1.39$  on day 30,  $10.04 \pm 1.47$  on day 60, and  $11.92 \pm 1.43$  by day 90 ( $p < 0.01$ ). The ST scores for this group also showed significant enhancement (Table 1). By day 90, these scores were at  $4.69 \pm 6.03$  for OSDI and  $0.44 \pm 0.74$  for

NPRS, indicating a significant downward trend ( $p < 0.01$ ) (Figure 4).

Mean TBUT at day 15 was  $5.70 \pm 0.61$  in males and  $4.98 \pm 1.02$  in females which improved significantly on repeated follow-ups ( $p < 0.01$ ), but the highest improvement was observed in males on day 90 in comparison to females. Likewise, ST score was improved significantly in males and females with better results in males on day 90. On the other hand, OSDI and NPRS scores were significantly decreased over time ( $p < 0.01$ ) (Table 2).

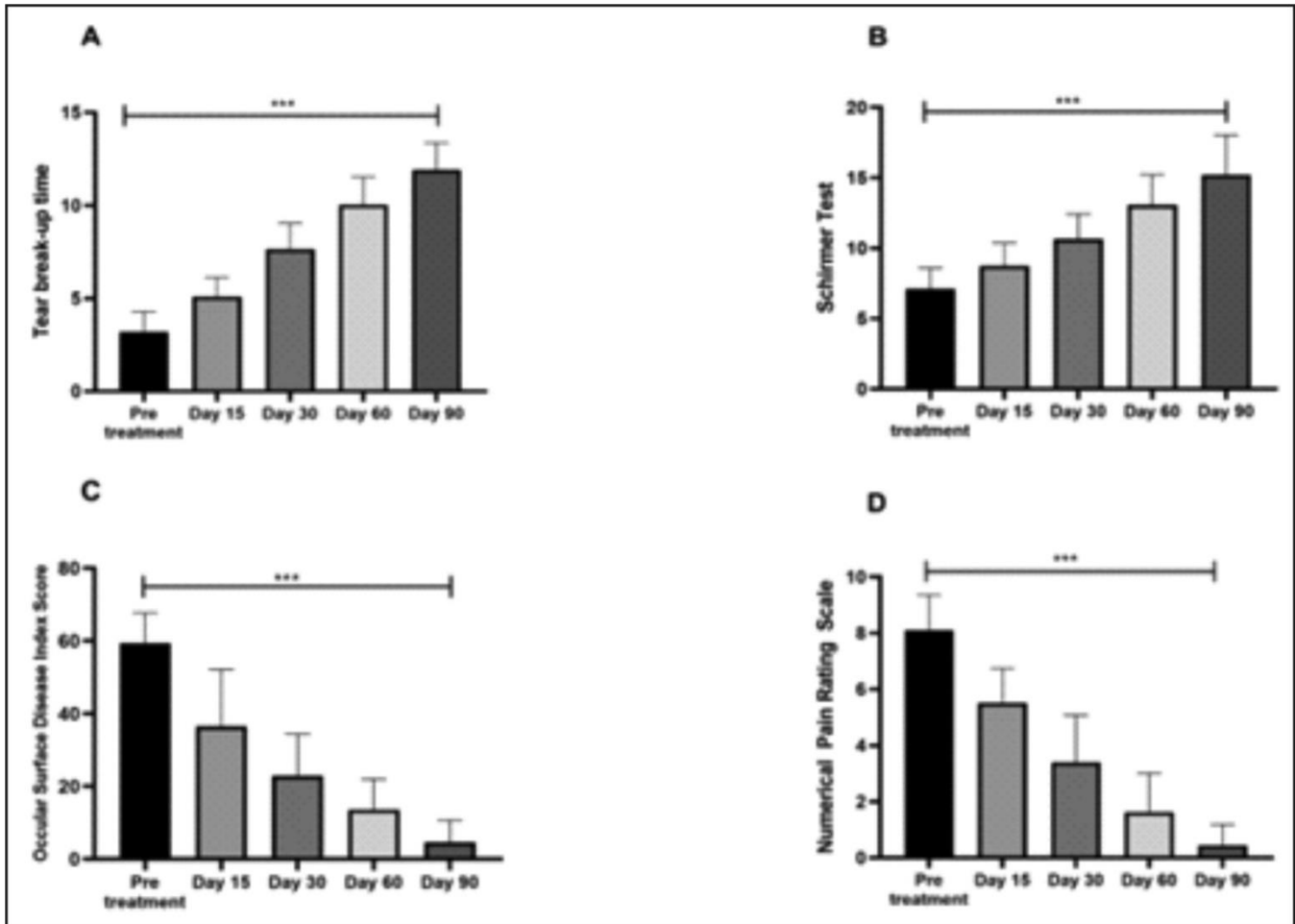
Based on age, TBUT and ST scores were improved significantly in both age groups ( $p < 0.01$ ). NPRS and OSDI scores were significantly reduced in both age groups with improved results in patients aged  $< 35$  years (Table 3).



**Figure 3:** Comparison of effects produced with and without vitamin D supplements on non-Sjogren dry eye over time (A) Tear break-up time (TBUT) was increased in group 2 having vitamin D supplement on day 15, 30, 60 and 90 as compared to group 1 having conventional dry eye treatment ( $p < 0.01$ ) (B) Schirmer's test (ST) score was also improved in group 2 in comparison with group 1 on day 15, 30, 60 and 90 ( $p < 0.01$ ). (C) Ocular surface disease index (OSDI) score was reduced in both groups on day 15, 30, 60 and 90 ( $p = 0.985$ ,  $p = 0.897$ ,  $p = 0.931$  and  $p = 0.656$  respectively). (D) Numerical pain rating scale (NPRS) score was also decreased in both groups on day 15, 30, 60 and 90 ( $p = 1.000$ ,  $p = 0.900$ ,  $p = 0.790$  and  $p = 0.730$  respectively).

**Table 1:** Supplementation effect on dry eyes over different time periods.

	Pre-treatment (n=54)		Post Treatment (n=54)			p-value
	Mean $\pm$ SD	Day 15 Mean $\pm$ SD	Day 30 Mean $\pm$ SD	Day 60 Mean $\pm$ SD	Day 90 Mean $\pm$ SD	
<b>TBUT</b>	$3.20 \pm 1.06$	$5.11 \pm 0.99$	$7.65 \pm 1.39$	$10.04 \pm 1.47$	$11.92 \pm 1.43$	$< 0.01$
<b>ST</b>	$7.12 \pm 1.44$	$8.76 \pm 1.60$	$10.66 \pm 1.74$	$13.09 \pm 2.11$	$15.22 \pm 2.79$	$< 0.01$
<b>OSDI</b>	$59.48 \pm 8.18$	$36.51 \pm 15.66$	$23.01 \pm 11.36$	$13.64 \pm 8.44$	$4.69 \pm 6.03$	$< 0.01$
<b>NPRS</b>	$8.11 \pm 1.25$	$5.51 \pm 1.22$	$3.40 \pm 1.66$	$1.63 \pm 1.37$	$0.44 \pm 0.74$	$< 0.01$



**Figure 4:** Effects of vitamin D3 supplements on non-Sjogren dry eye over time **(A)** Tear break-up time (TBUT) score was significantly improved over time ( $p < 0.01$ ) **(B)** Schirmer's test (ST) score was significantly improved over time ( $p < 0.01$ ) **(C)** Ocular surface disease index (OSDI) score was significantly reduced after repeated follow-ups ( $p < 0.01$ ) **(D)** Numerical pain rating scale (NPRS) score was significantly reduced after repeated follow-ups ( $p < 0.01$ ).

**Table 2:** Effect of vitamin D supplements on non-Sjogren dry eye over time based on gender.

		Post Treatment (n=54)				
		Day 15	Day 30	Day 60	Day 90	p-value
		Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
TBUT	M	5.70±0.61	8.20±1.04	10.54±0.58	12.08±0.08	<0.01
	F	4.98±1.02	7.53±1.43	9.93±1.59	11.89±1.59	<0.01
ST	M	10.20±1.03	11.60±0.51	14.60±0.51	17.20±2.86	<0.01
	F	8.43±1.53	10.45±1.86	12.75±2.19	14.77±2.60	<0.01
OSDI	M	21±5.16	12.50±10.76	9.99±8.60	0±0	<0.01
	F	40.04±15.10	25.39±10.16	14.46±8.27	5.75±6.21	<0.01
NPRS	M	4±0	1.20±1.03	0.20±0.42	0±0	<0.01
	F	5.86±1.09	3.90±1.34	1.95±1.31	0.54±0.79	<0.01

M, male; F, female; TBUT, tear break-up time; ST, Schirmer's test; OSDI, ocular surface disease index; NRPS, numerical pain rating scale

## DISCUSSION

Our results showed that Vitamin D supplementation had significant effects in improving ST and TBUT as compared to the conventional treatment group. Studies

have shown that inflammation is the core mechanism of DED triggered by tear hyperosmolarity.<sup>16</sup> It results either from decreased production or increased evaporation of tears and cause damage to ocular

**Table 3:** Effect of vitamin D supplements on non-Sjogren dry eye over time based on age group.

		Post Treatment (n=54)				p-value
		Day 15 Mean ± SD	Day 30 Mean ± SD	Day 60 Mean ± SD	Day 90 Mean ± SD	
TBUT	<35	5.08±0.54	7.62±0.90	9.90±1.22	11.44±0.71	<0.01
	≥35	5.13±1.24	7.67±1.67	10.14±1.64	12.28±1.72	<0.01
ST	<35	8.70±1.14	10.78±1.27	13.47±1.53	15.69±2.60	<0.01
	≥35	8.81±1.88	10.58±2.04	12.80±2.44	14.87±2.91	<0.01
OSDI	<35	31.78±18.44	18.32±12.06	8.29±7.37	0.13±0.34	<0.01
	≥35	40.03±12.40	26.49±9.59	17.60±6.90	8.07±6.03	<0.01
NPRS	<35	5.26±0.91	2.74±1.57	0.78±0.67	0±0	<0.01
	≥35	5.71±1.39	3.90±1.58	2.25±1.43	0.77±0.84	<0.01

TBUT, tear break-up time; ST, Schirmer's test; OSDI, ocular surface disease index; NRPS, numerical pain rating scale

surface. Any inflammatory change is the core driver in pathophysiology of dry eye.<sup>17</sup> Vitamin D deficiency is highly prevalent condition with worldwide prevalence of almost one billion.<sup>18</sup> Relationship between DED and vitamin D deficiency has been documented by various studies.<sup>19</sup> However, few conflicting studies showed no association between them.<sup>20</sup> Vitamin D receptors are present in various ocular structures and have ability to convert its inactive form into an active vitamin D.<sup>11</sup>

The current study, provides some important insight on the possible advantages of vitamin D3 therapy in DED. As there were no appreciable variations in the mean ages of the study participants in Groups 1 and 2, it reduces the likelihood that age would have a confounding effect on the study findings. No statistically significant differences were found between Group 1 and Group 2 regarding vitamin D level.

Our study showed multiple measurements of all dry eye indicators at subsequent follow ups indicating subsequent improvement in signs and symptoms of the disease.

The outcomes of TBUT, ST, OSDI and NPRS score showed that Groups 1 and 2 both had lower OSDI and NPRS scores following the intervention. These results imply that among non-Sjögren dry eye patients with low serum Vitamin D levels, Vitamin D3 treatment may be helpful in improving the symptoms of dry eye and related pain. Group 2, which got Vitamin D3 supplementation, showed an improvement in both TBUT and ST scores, while Group 1 showed no discernible changes. These results imply that in non-Sjögren dry eye patients with low serum Vitamin D levels, Vitamin D3 therapy may improve tear film integrity and tear production.

In the present study, mean age of patients was comparable to already published research where the

mean age was 36.8±8.56 years in cases and 34.8±10.13 years in control group.<sup>21</sup> This study was conducted on 108 subjects however reference study included 100 participants. Both studies were clinical trials with difference in time of supplementation dosage. In this study, patients were assessed on repeated follow-up whereas participants of reference study were assessed only after 8 weeks of supplementation.<sup>21</sup> Similarly, mean serum of vitamin D level was 15.0341±3.27 in group 1 and 14.9330±3.26 in group 2. The present study delves into the effect of Vitamin D3 supplementation on NSDE patients. Evidently, the consistent rise in TBUT and ST scores for Group 2 over the 90-day period underscores the potential therapeutic benefits of Vitamin D3 for NSDE patients. TBUT is a crucial parameter that indirectly indicates the stability of the tear film. An increase in TBUT denotes a potential improvement in tear film stability, which is essential for maintaining ocular surface health. The significant enhancement in TBUT in Group 2 might suggest the role of Vitamin D3 in enhancing tear film stability, which can potentially reduce dry eye symptoms.

Another study showed similar results when TBUT was measured after 8, 12 and 24 weeks but it included only 40 participants.<sup>21</sup> All participants in this study were DED patients with vitamin D level less than 25ng/ml however the referenced study included vitamin D deficient individuals having serum level less than 20 ng/ml with disease of meibomian gland either with DES or without DES.

Study of Bae et al., showed significant results after initial follow-ups of 2 and 6 weeks but results were non-significant after 10 weeks of vitamin D supplementation.<sup>14</sup> This study included 105 participants and was retrospective observational study in contrast to present study which is a prospective

clinical trial.

Karaca et al, showed similar results with ST score of  $17.33 \pm 7.29$  after 24 weeks of vitamin D supplementation.<sup>22</sup> Contrary to that, study of Hwang et al., showed non-significant results after oral and intramuscular (IM) supplementation.<sup>23</sup> Main difference between two studies was age group which influences signs and symptoms of disease. Age group in this study was 20-50 years whereas study of Hwang et al, included patients with 23–84 years. Signs and symptoms of dry eyes are more severe in older age group due to various risk factors which ultimately affect results. Further, the ST score is a measure of tear production. The significant rise in ST scores for Group 2 indicates that Vitamin D3 might have a role in stimulating or enhancing tear production, leading to a more lubricated ocular surface. This is especially pertinent given the existing literature suggesting the anti-inflammatory properties of Vitamin D3, which may contribute to improved lacrimal gland function.

Present study showed significant improvement in males and females after using vitamin D supplementation. Bae et al,<sup>14</sup> showed non-significant results after repeated follow-ups. They had included patients with older aged group and did not exclude metabolic disorders, various systemic diseases and postmenopausal women. These confounding factors might be responsible for contrasting results. Study conducted by Watts et al, showed significant improvement in TBUT and ST score on repeated follow-ups.<sup>10</sup> This study excluded endocrine and metabolic disorders, systemic disease and postmenopausal estrogen therapy which were not considered in previous study.

Similarly, NPRS and OSDI scores were used to determine severity of DED symptoms. OSDI and NPRS scores were decreased in both groups. OSDI score was also reduced in another study after vitamin D supplements.<sup>22</sup>

Oral vitamin D3 supplementation played a significant role in DED treatment by improving TBUT and Schirmer's tear test score and by decreasing NPRS and OSDI scores. While OSDI and NPRS scores also witnessed a decline, indicating an overall subjective improvement in dry eye symptoms from the patient's perspective, it's crucial to understand the underlying mechanisms. Vitamin D3 might not only be acting at the ocular surface level but also at a systemic level, potentially modulating immune responses and

reducing inflammation, a key component in dry eye syndrome.

Oral vitamin D3 supplementation may serve as a promising treatment option for NSDE disease associated with hypovitaminosis D.

Limitations of the study include small sample and short follow up. It is necessary to do additional research with larger sample sizes and longer follow-up in order to confirm and further elaborate the findings. Certain confounding factors such as socioeconomic status, coffee use, profession, and sun exposure, were not considered in our study. As this is not the population-based study so results must be interpreted with caution. Future studies may focus on exploring the cellular and molecular mechanisms at play, giving more profound insights into the potential of Vitamin D3 as a therapeutic agent for NSDE.

## REFERENCES

1. **Rouen PA, White ML.** Dry eye disease: prevalence, assessment, and management. *Home Healthc. Now.* 2018;**36(2)**:74-83. Doi:10.1097/NHH.0000000000000652
2. **Giannaccare G, Ghelardini C, Mancini A, Scorcia V, Di Cesare Mannelli L.** New perspectives in the pathophysiology and treatment of pain in patients with dry eye disease. *J Clin Med.* 2021;**11(1)**:108. Doi:10.3390/jcm11010108
3. **Liu J, Dong Y, Wang Y.** Vitamin D deficiency is associated with dry eye syndrome: a systematic review and meta-analysis. *Acta Ophthalmol.* 2020;**98(8)**:749-754. Doi:10.1111/aos.14470
4. **Shimazaki J.** Definition and diagnostic criteria of dry eye disease: historical overview and future directions. *Invest Ophthalmol Vis Sci.* 2018;**59(14)**:DES7-12. Doi:10.1167/iops.17-23475
5. **Gomes JA, Santo RM.** The impact of dry eye disease treatment on patient satisfaction and quality of life: A review. *Ocul Surf.* 2019;**17(1)**:9-19. Doi:10.1016/j.jtos.2018.11.003
6. **Chaudhary B.** Vitamin D deficiency in Rawalpindi-Islamabad region. *J Rawalpindi Med.* 2017;**21(2)**:169-172.
7. **Vranić L, Mikolašević I, Milić S.** Vitamin D deficiency: consequence or cause of obesity?. *Medicina.* 2019;**55(9)**:541. Doi: 10.3390/medicina55090541
8. **Willcox MD, Argüeso P, Georgiev GA, Holopainen JM, Laurie GW, Millar TJ, et al.** TFOS DEWS II tear film report. *Ocul Surf.* 2017;**15(3)**:366-403. Doi:10.1016/j.jtos.2017.03.006



9. **Kurtul BE, Özer PA, Aydinli MS.** The association of vitamin D deficiency with tear break-up time and Schirmer testing in non-Sjögren dry eye. *Eye*. 2015;**29(8)**:1081-1084. Doi:10.1038/eye.2015.96
10. **Watts P, Sahai A, Kumar PR, Shamsad MA, Trivedi GK, Tyagi L.** A prospective study to assess the role of vitamin D individually and in combination with cyclosporine in the treatment of dry eye in patients with deficient serum 25 (OH) D levels. *Indian J Ophthalmol*. 2020;**68(6)**:1020. Doi: 10.4103/ijo.IJO\_1492\_19
11. **Kizilgul M, Kan S, Ozcelik O, Beysel S, Apaydin M, Ucan B. et al.** Vitamin D replacement improves tear osmolarity in patients with vitamin D deficiency. *Semin Ophthalmol*. 2018;**33(5)**:589-594. Doi:10.1080/08820538.2017.1358752
12. **Lu X, Elizondo RA, Nielsen R, Christensen EI, Yang J, Hammock BD. et al.** Vitamin D in tear fluid. *Invest Ophthalmol*. 2015;**56(10)**:5880-5887. Doi:10.1167/iovs.15-17177
13. **Lin Y, Ubels JL, Schotanus MP, Yin Z, Pintea V, Hammock BD. et al.** Enhancement of vitamin D metabolites in the eye following vitamin D3 supplementation and UV-B irradiation. *Curr Eye Res*. 2012;**37(10)**:871-878. Doi: 10.3109/02713683.2012.688235
14. **Bae SH, Shin YJ, Kim HK, Hyon JY, Wee WR, Park SG.** Vitamin D supplementation for patients with dry eye syndrome refractory to conventional treatment. *Sci*. 2016;**6(1)**:33083. Doi:10.1038/srep33083
15. **Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al.** Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2011;**96(7)**:1911-1930. Doi: 10.1210/jc.2011-0385
16. **Baudouin C, Aragona P, Messmer EM, Tomlinson A, Calonge M, Boboridis KG. et al.** Role of hyperosmolarity in the pathogenesis and management of dry eye disease: proceedings of the OCEAN group meeting. *Ocul Surf*. 2013;**11(4)**:246-258. Doi: 10.1016/j.jtos.2013.07.003
17. **Guzmán M, Miglio M, Keitelman I, Shiromizu CM, Sabbione F, Fuentes F. et al.** Transient tear hyperosmolarity disrupts the neuroimmune homeostasis of the ocular surface and facilitates dry eye onset. *J Immunol*. 2020;**161(2)**:148-161. Doi: 10.1111/imm.13243
18. **Sizar O, Khare S, Goyal A, Givler A.** Vitamin D deficiency. 2022. PMID: 30335299.
19. **Jin KW, Ro JW, Shin YJ, Hyon JY, Wee WR, Park SG.** Correlation of vitamin D levels with tear film stability and secretion in patients with dry eye syndrome. *Acta Ophthalmol*. 2017;**95(3)**:e230-235. Doi: 10.1111/aos.13241
20. **Jeon DH, Yeom H, Yang J, Song JS, Lee HK, Kim HC.** Are serum vitamin D levels associated with dry eye disease? Results from the study group for environmental eye disease. *J Prev Med Publ Health*. 2017;**50(6)**:369. Doi: 10.3961/jpmph.17.089
21. **Najjaran M, Zarei-Ghanavati S, Arjmand Askari E, Eslampoor A, Ziaei M.** Effect of oral vitamin D supplementation on dry eye disease patients with vitamin D deficiency. *Clin Exp Optom*. 2023;**106(3)**:257-262. Doi: 10.1080/08164622.2022.2033601
22. **Karaca EE, Kemer ÖE, Özek D, Berker D, Imga NN.** Clinical outcomes of ocular surface in patients treated with vitamin D oral replacement. *Arq Bras*. 2020;**83**:312-317. Doi: 10.5935/0004-2749.20200043
23. **Hwang JS, Lee YP, Shin YJ.** Vitamin D enhances the efficacy of topical artificial tears in patients with dry eye disease. *Cornea*. 2019;**38(3)**:304-310. Doi: 10.1097/ICO.0000000000001822

### Authors Designation and Contribution

Bushra Kanwal; Optometrist: *Concepts, Design, Literature search, Manuscript preparation, Manuscript editing, Manuscript review.*

Ayesha Kiran; Optometrist: *Concepts, Design, Data acquisition, Data analysis, Statistical analysis.*

Muhammad Junaid Iqbal; Phd Scholar: *Data analysis, Statistical analysis, Manuscript review.*

Iqra Khalil; Optometrist: *Manuscript preparation, Manuscript editing, Manuscript review.*

Aghna Maryam; Phd Scholar: *Manuscript preparation, Manuscript editing, Manuscript review.*

