

# The Relation between Serum Level of Vitamin D and Dry Eye Disease

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## Abstract

**Purpose:** To investigate the relation between serum level of vitamin D and dry eye disease.

**Patients and Methods:** In this cross-sectional case-control study, 40 patients with dry eye disease were enrolled. Dry eye was diagnosed based on the slit lamp examination, tear meniscus height, tear break up time test, ocular surface disease index, and the results of Schirmer test. Forty age and sex matched healthy individuals served as controls. The serum level of vitamin D was measured and compared between patients with dry eye disease and controls.

**Results:** The mean age was  $44.92 \pm 11.4$  and  $44.07 \pm 11.29$  years in the case and control groups, respectively ( $P = 0.739$ ). The mean serum level of vitamin D was  $21.18 \pm 11.83$  ng/dl in the case group and  $20.54 \pm 9.98$  ng/dl in the control group ( $P = 0.793$ ). Ocular surface disease index had a positive correlation with age ( $r = +0.363$ ,  $P < 0.0001$ ), but a negative correlation with the serum level of vitamin D ( $r = -0.480$ ,  $P = 0.002$ ). Other investigated test results failed to demonstrate an association between vitamin D deficiency and dry eye.

**Conclusion:** According to the present study results, no significant association between vitamin D deficiency and dry eye was detected. However, due to relatively small sample size in the present study further studies are recommended to better investigate this subject.

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## Introduction

Dry eye disease (DED) is prevalent among the elderly, affecting 33 % of the world population<sup>1</sup>. Approximately, 5 million people in the US above the age of 50 suffer from DED, with women affected more frequently compared to men<sup>1</sup>. Dry eye occurs due to tear deficiency or excessive tear evaporation<sup>1</sup>.

The most annoying symptoms are ocular discomfort, blurred vision and pain, which sometimes lead to depression and social problems<sup>2,3</sup>. Hyperosmolarity of the tear due to either tear deficiency or excess evaporation may damage the corneal epithelial cells and lead to subsequent liberation of miscellaneous inflammatory cytokines and matrix metalloproteinases<sup>5</sup>. This vicious cycle can further destruct the epithelium and exacerbate the dry eye<sup>5,6</sup>.

Dry eye is related to a complex of localized autoimmune reactions with inflammatory properties and vitamin D is a well-known immunomodulatory and anti-inflammatory agent, which might potentially be able to reverse the processes of dry eye<sup>7</sup>. On the other hand, vitamin D deficiency might be reasonably an important cause of dry eye. Previous studies have reported inconsistent results regarding the vitamin D deficiency and DED, so the present case-control study was performed to further evaluate their relation.

## Patients and Methods

In this case-control study, patients with chief complaint of burning, itching and foreign body sensation were visited in an ophthalmology clinic and dry eye was confirmed in 40 of them. The control group included 40 sex and age matched healthy individuals recruited from the optometry department.

Exclusion criteria were rheumatologic diseases, malignancy, previous corneal surgery, chronic

ocular diseases, malnutrition, contact lens use and consumption of some medications such as three-cyclic antidepressants,  $\beta$ -blockers, diuretics, anti histamines and anti glaucoma medication.

The study was performed with compliance to the tenets of the declaration of Helsinki and an informed consent was signed by all participants. The study was approved by the ethics committee of Shahid Beheshti University of Medical Sciences, Tehran, Iran. A questionnaire was designed and the demographic information, history of systemic and ocular diseases, drug history, ocular symptoms (burning, foreign body sensation, tearing, itching, discharge, dry eye sensation, photophobia, pain, blinking discomfort and red eye) were recorded. Patients were examined by a single ophthalmologist (SF), in the same room under stable conditions.

All cases underwent complete ophthalmologic examination including BCVA, slit lamp examination, tonometry, and funduscopy.

DED was diagnosed based on slit-lamp examination and the results of Schirmer, tear meniscus height (TMH), and tear break up time (TBUT) tests. To perform the Schirmer test a strip of filter paper was placed without anesthetic in the inferior cul-de-sac for 5 minutes, and the amount of wetting was recorded. The normal amount is approximately 15 mm. The wetting length shorter than 5 mm was regarded to be a dry eye determinant<sup>8</sup>. TMH was evaluated by measuring the height of the tear meniscus from eye lid edge in the area of the pupil. A tear meniscus of 0.3 mm or less was considered abnormal<sup>8</sup>. TBUT was determined by instilling fluorescein, and then evaluating the stability of the tear film. The examiner moistened a fluorescein strip with sterile saline and applied it to the tarsal conjunctiva without any anesthetic drop

utilization. After several blinks, the tear film was examined using a broad beam of the slit lamp with a blue filter. The time lapse between the last blink and the appearance of the first randomly distributed dry spot in the cornea was recorded as the tear breakup time. TBUT result of less than 10 sec was considered abnormal <sup>8</sup>.

Ocular surface disease index (OSDI) as a major dry eye questionnaire consists of 12 questions related to the dry eye symptoms and scores 0 to 4 for each question. Sum of the total scores is multiplied by 25 and then divided by 12. This final score would be 0 to 100 and the higher scores reflect a worse dry eye condition. This questionnaire is considered as an accepted method for dry eye evaluation in terms of validity and reliability <sup>8</sup>.

After determination of dry eye severity using OSDI test, 0.5 ml of patient's blood was taken from the right decubitus vein and the vitamin D level was checked in the laboratory. Serum level of vitamin D above 30 ng/dl was regarded to be normal, while, lower than 20 ng/dl was considered Vitamin D deficiency <sup>8</sup>.

### Statistical Analysis

All statistical analysis was performed using SPSS statistical package version 22.0 (Armonk, NY: IBM Corp) and a P value of less than 0.05 was considered statistically significant. Descriptive statistics were used to present

central tendency and dispersion. Student T test and Pearson correlation coefficient were used to compare the results between the study groups. Chi-Square test was applied to analyze the qualitative data.

### Results

Eighty participants including 40 patients with DED and 40 normal control individuals were enrolled in the study. Male/female ratio was 24/16 in each group. The mean ages of participants was  $44.92 \pm 11.4$  and  $44.07 \pm 11.29$  in the case and control groups, respectively ( $P = 0.739$ ) (Table 1). The mean OSDI scores were  $65.74 \pm 9$  and  $34.25 \pm 12.86$  in the case and control groups respectively ( $P < 0.001$ ).

The majority of the participants in both groups suffered from vitamin D insufficiency (Figure 1). The mean serum level of vitamin D was  $21.18 \pm 11.83$  and  $20.54 \pm 9.98$  ng/dl in the case and control groups indicating no statistically significant difference ( $P = 0.793$ ) (Table 2). The relation between vitamin D serum level and DED was also evaluated in three age subgroups (below 40, 40-50, above 50 years). There was no statistically significant difference regarding the serum levels of vitamin D when comparing the case and control groups in any of these age groups (Table 2). The correlations between three main quantitative data (Age, OSDI and vitamin D serum level) were investigated in

**Table 1: Demographic findings of patients entering the study**

Variable	Group	Mean $\pm$ SD	P value *
Age	Case	$44.92 \pm 11.4$	0.739
	Control	$44.07 \pm 11.29$	
OSDI	Case	$65.74 \pm 9$	0.001
	Control	$34.25 \pm 12.86$	

\* Independent T test,

OSDI: Ocular Surface Disease Index.

**Table 2: The mean vitamin D serum levels in case and control groups**

Age (Years)	Groups	Number	Vitamin D (ng/dl) Mean ± SD	P value*
All Ages	Case	40	21.18 ± 11.83	0.793
	Control	40	20.54 ± 9.98	
Below 40	Case	10	24.62 ± 10.88	0.105
	Control	14	18.1 ± 5.16	
40-50	Case	16	23.5 ± 14.03	0.854
	Control	14	22.62 ± 11.48	
Over 50	Case	14	16.07 ± 8.2	0.243
	Control	12	20.94 ± 12.36	

\* Independent T test

all study participants (Table 3). According to our findings, a significant positive correlation was detected between age and OSDI index (Pearson correlation; + 0.363,  $P < 0.0001$ ) and a significant negative correlation was observed between OSDI index and serum level of vitamin D (Pearson correlation; - 0.480,  $P = 0.002$ ) (Table 3).

### Discussion

In the present study, vitamin D serum level was not statistically different between case (dry eye) and control groups even after age and gender adjustment.

Similar to our findings Jeon et al.,<sup>9</sup> in a recent study did not find a statistically significant relation between blood vitamin D levels and

**Table 3: Correlation between quantitative data (Age, OSDI and vitamin D serum level) of all patients entering the study**

Variable		Age	OSDI	Vitamin D
Age	Pearson Coefficient	-	0.363 *	- 0.185
	P value**	-	< 0.0001	0.254
OSDI	Pearson Coefficient	0.363	-	- 0.480
	P value**	< 0.0001	-	0.002
Vitamin D	Pearson Coefficient	- 0.185	- 0.480 **	-
	P value**	0.254	0.002	-

\* Pearson correlation

\*\* P value < 0.01 level (2-tailed)

DED. In another study by Jee et al.,<sup>10</sup> a total of 16,396 participants aged > 19 years were randomly selected and the relation between serum vitamin D levels and DED was investigated. They did not find a statistically significant association between blood vitamin D levels and DED<sup>10</sup>. Similarly Kim et al.,<sup>11</sup> reported that vitamin D deficiency was associated with dry eye in an unadjusted model, but the association was not statistically significant after adjustment.

In contrast to our results, some previous studies performed to evaluate the relation between vitamin D serum levels and DED have indicated an association. Yildirim et al.,<sup>12</sup> assessed fifty premenopausal women with vitamin D deficiency (serum vitamin D levels < 20 ng/mL) and 48 controls. The association of vitamin D deficiency and worse Schirmer, TBUT and OSDI index were evaluated and statistically significant correlations were found between each of these parameters and serum vitamin D deficiency<sup>12</sup>. They concluded that dry eye and impaired tear function in patients with vitamin D deficiency may indicate a protective role for vitamin D in the development of dry eye<sup>12</sup>. In another case-control study including 70 DED cases and 70 healthy controls, by Meng et al.,<sup>13</sup> 25 (OH) D levels were lower in patients with DED compared to controls. They also found that there were statistically significant associations between serum 25 (OH) D levels and Schirmer test, TBUT, and OSDI results<sup>13</sup>. Also Kurtul et al.,<sup>1</sup> have reported lower serum level of vitamin D in cases with dry eye.

There are also some studies that have assessed the effect of vitamin D supplementation on dry eye. Yang et al.,<sup>14</sup> have reported that vitamin D supplement improves dry eye symptoms, tear quality and ocular surface conditions among patients with vitamin D deficiency. Bae et al.,<sup>15</sup> analyzed the relation between the severity of dry eye (based on TBUT, tear secretion test, Fluorescein staining test and OSDI) and serum levels of 25 OH-vitamin D in patients with refractory dry eye. After treatment with intramuscular vitamin D supplementation a significant improvement of ocular discomfort and lid margin hyperemia were observed at 2<sup>nd</sup>, 6<sup>th</sup> and 10<sup>th</sup> weeks after commencement of therapy.

The negative correlation between vitamin D serum level and OSDI observed in the present study could be interpreted in favor of a possible association between dry eye symptoms and vitamin D deficiency, but we could not find a significant difference in vitamin D serum level between the case and control groups.

The main limitation of our study was the relatively small sample size. Also majority of participants either in case or control group suffered from vitamin D insufficiency which can confound our outcomes.

### Conclusion

According to the present study results, no significant association between vitamin D deficiency and dry eye was detected. However, due to relatively small sample size in the present study further studies are recommended to better investigate this subject.

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## Footnotes and Financial Disclosures

### Conflict of interest:

The authors have no conflict of interest with the subject matter of the present study.