Original Article

Vitamin D Status Among Patients With Dry Eye Syndrome Attended In Bangabandhu Sheikh Mujib Medical University (BSMMU)

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Abstract

Background: Dry eye syndrome (DES) is a common ocular manifestation. Artificial tears provide relief of eye irritation in patients with aqueous tear deficiency, but do not treat the underlying inflammation in Dry eye syndrome. Aim: To assess the vitamin D status of the dry eye syndrome patients.

Methodology: This cross-sectional study was conducted in the Department of Community Ophthalmology, BSMMU, Shahbag, Dhaka, from July 2019 to June 2020. Within the period a total of 50 cases of dry eye syndrome patients that met the inclusion criteria were taken as samples after receiving their informed consent. Detailed history, physical examination and Ophthalmological examination including Tear film Breakup Time (TBUT) of each patient was performed and recorded. Eye discomfort was assessed by the Ocular Surface Disease Index (OSDI) the score of which ranges from 0 to 100. A score of 12 was used as a cutoff for normal, 13-22 for mild dry eye, 23-32 for moderate dry eye, and ≥ 33 for severe dry eye. Tear film Breakup Time (TBUT) <10 s was taken as abnormal.

Results: In this study, mean (±SD) fluorescein Tear film Breakup Time (TBUT) was 5.89±1.31 sec, Schirmer test without anesthesia was 7.45±2.31mm/5 min, Schirmer test with anesthesia was 9.06±2.06mm/5 min and Ocular Surface Disease Index (OSDI) was 34.44±5.64. Mean (±SD) serum vitamin D level ng/mL was 5.89±1.31 ng/mL. 14 (28%) cases were found as insufficient, 33 (66%) cases were deficient and only 3 (6%) cases found to have normal Vitamin D status. Vitamin D level was positively correlated with Tear Breakup Time (TBUT), Schirmer test1 and Schirmer test2 and negatively correlated with OSDI. This correlation was statistically significant for Tear film Breakup Time (TBUT), Schirmer test2 and Ocular Surface Disease Index (OSDI).

Conclusion: Vitamin-D deficiency appears to have an effect on ocular surface parameters in patients with dry eye syndrome.

Key words: Dry eye syndrome, Vitamin D, Fluorescein, Tear film Breakup Time (TBUT), Schirmer test, Ocular Surface Disease Index (OSDI).

Introduction

Dry eye syndrome (DES) is accompanied by tear instability, increased osmolarity of the tear film and ocular surface inflammation. The common symptoms of dry eye are ocular discomfort, soreness, redness, ocular fatigue, sensitivity to light and blurred vision.[1] It is a consequence of reduced tear secretion by the lacrimal glands or increased tear evaporation.[2] 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. This vicious cycle can further destruct the epithelium and exacerbate the dry eye.[3] 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.[4]

Several studies found have larger amounts of vitamin D in tear fluid obtained directly from lacrimal and accessory glands compared to plasma concentration. Megalin and cubilin are vitamin D transporters. They are expressed in lacrimal and accessory glands and are responsible for producing tear fluid.[5] The vitamin D receptors are present in the corneal epithelium,

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endothelium and retinal pigmentary epithelium. Vitamin D strengthened the corneal epithelial barrier.[2,6] Hence, vitamin D deficiency might be reasonably an important cause of dry eye.

Dry eye syndrome is prevalent among the elderly, affecting 33% of the world population.[3] Various researchers of different countries had suggested that there was a relationship between dry eye syndrome and vitamin D deficiency. [1,7] But no published data are available in our country regarding this topic. Therefore, the present study had been designed to assess the vitamin D status among the dry eye syndrome patient. The findings may be helpful as background information for better management of the patients suffering from dry eye.

Methodology

This cross-sectional study was conducted in the Department of Community Ophthalmology, BSMMU, Shahbag, Dhaka from July 2019 to June 2020. A total 50 of cases of dry eye syndrome that met the inclusion criteria were taken as samples after receiving the patient's informed consent. Ethical clearance was obtained from the Institutional Review Board (IRB) of Bangabandhu Sheikh Mujib Medical University (BSMMU). Detailed history and physical examination of each patient were performed and recorded. Visual acuity was assessed by Snellens chart and the anterior segment of the eye was examined with slit lamp biomicroscope to know the condition of eyelid, meibomian glands, conjunctival surface and cornea. Eye discomfort was assessed by the ocular surface disease index (OSDI). The OSDI questionnaire was accustomed to quantify dry eye symptoms. Subjects were asked questions regarding the dry eye symptoms that they had experienced during a one-week recall period. The OSDI questions consisted of three subscales – ocular symptoms, vision-related functions and environmental triggers. Each answer was scored on a 4-point scale from zero (indicating no problems) to four (indicating a significant problem).

Responses to all of the questions were combined to generate a composite OSDI score that ranged from 0 to 100. A score of 12 was used as a cutoff for normal, 13–22 for mild dry eye, 23–32 for moderate dry eye, and ≥ 33 for severe dry eye. [8] Tear film evaluations were done by measurement of Tear film Breakup Time (TBUT) and Schirmers Test (SchT). A dry fluorescein strip was touched to the inferior fornix with the patient instructed to look up. The corneal surface was seen under slit lamp biomicroscope with low magnification using a cobalt blue filtered light. The patient was asked to blink once and look straight without blinking.

The time of appearance of first small black spot within blue field (dry spot) from the last blink was measured. The TBUT less than 10 seconds was taken as abnormal. Without previously instilling anesthetic drops, the chirmer strips (Tianjin Jingming New Technological Development Co., Ltd, China) were inserted into the lower conjunctival sac at the junction of the lateral and middle third, avoiding touching the cornea and the length of wetting strips in millimeters was recorded after 5 minutes for Schimer-I. 15 minutes later, strips were placed over the same point in the same person again for 5 minutes, after installation of topical anesthesia with 0.5% proparacaine hydrochloride eye drops (Alcon laboratories Inc., s.a. Alcon-Couvreur n.v.) twice at 1 minute interval and then the length of wetting was read for Schimer-II.

5ml of venous blood sample was collected from the antecubital vein and sent to the Department of Biochemistry, BSMMU for estimation of serum vitamin D levels. Serum Vitamin D level < 20 ng/ml was considered to be vitamin D deficiency, 21-29 ng/ml was considered to be insufficient and a level > 30 ng/ml was considered to be normal.[9] All the information was recorded in a prefixed questionnaire. Data was analyzed statistically by using Statistical Package for Social Science (SPSS-26). The results were expressed as frequency, percentage and mean ± SD and level of significance was calculated at $p<0.05$. Z-proportion test was performed to compare between the groups. Pearson Correlation coefficient test was performed to observe the relation between dry eye and Vitamin D level.

Results

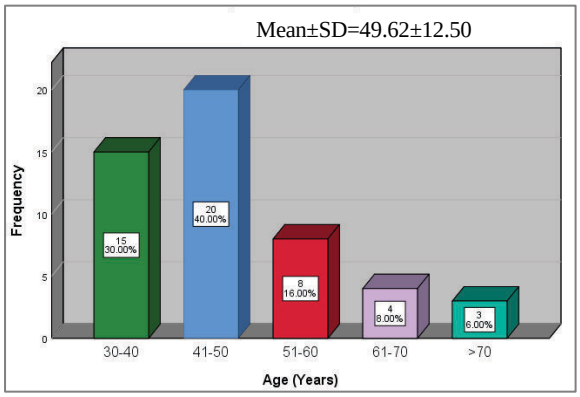

Fig 1: *Age distribution of Dry Eye Syndrome (DES) patients (n=50).*

Figure showd that mean±SD age was 49.62±12.50 years. Out of 50 patients 15 (30%) were 30-40 years of age, 20 (40%) were 41-50 years 8 (16%) were 51-60 years 4 (8%) were 61-70 years and 3 (6%) were >70 years. The youngest and the oldest patients were 30 and 91 years respectively.

Among 50 subjects, majority (62%) of the study subjects were female and only 38% were male.

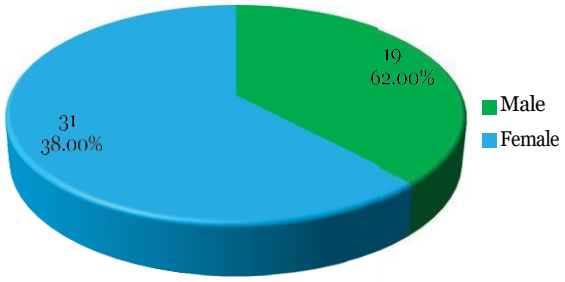

Fig 2: *Gender distribution of Dry Eye Syndrome (DES) patients (n=50).*

Table-I

Clinical characteristics of Dry Eye Syndrome (DES) patients (n=50).

Variable	Study subjects	Parameters
OSDI	34.44±5.64	Normal: 0 – 12 Mild: 13-22 Moderate: 23 -32 Severe: ≥ 33
Fluorescein TBUT (seconds)	5.89±1.31	Normal: ≥ 10 seconds Abnormal: < 10 seconds
Schirmer test 1 (mm/5 min)	7.45±2.31	Normal: 15 mm/5min Equivocal: 10 – 14 mm/5min Abnormal: < 10 mm/5min
Schirmer test 2 (mm/5 min)	9.06±2.06	Normal: 15 mm/5min Equivocal: 10 – 14 mm/5min Abnormal: < 10 mm/5min

*Data were expressed as Mean±SD.
*TBUT= Tear film Breakup Time
*Schirmer test 1= Schirmer test without anesthesia,
*Schirmer test 2= Schirmer test with anesthesia, n=study subjects.

Table I showed mean (±SD) OSDI was 34.44±5.64, fluorescein TBUT was 5.89±1.31 sec, Schirmer test without anesthesia was 7.45±2.31mm/5 min and Schirmer test with anesthesia was 9.06±2.06mm/5 min.

Table-II

Serum vitamin D status of Dry Eye Syndrome (DES) patients (n=50).

Vitamin D status (ng/mL)		Study subjects
>30	Normal	3 (6%)
20-29	Insufficiency	14 (28%)
<20	Deficiency	33 (66%)
Mean±SD		5.89±1.31

*Data were expressed as Mean±SD

Table II revealed that mean (±SD) serum vitamin D level ng/mL was 5.89±1.31 ng/mL . 14 (28%) cases were found as insufficient, 33 (66%) cases were deficient and only 3 (6%) cases found as normal in their Vitamin D status.

Table-III

Association of vitamin D status with OSDI of Dry Eye Syndrome (DES) patients (n=50).

Vitamin D status (ng/mL)		OSDI			
		Normal eye (0-12)	Mild dry eye (13-22)	Moderate dry ey (23-32)	Severe dry eye (≥33)
Normal	>30	0 (0%)	3 (6%)	0 (0%)	0 (0%)
Insufficiency	20-29	0 (0%)	1 (2%)	6 (12%)	7 (14%)
Deficiency	<20	0 (0%)	0 (0%)	0 (0%)	33 (66%)

*Data were expressed as frequency and percentage.

*OSDI-Ocular Surface Disease Index

In the severe dry eye group, 7 (14%) cases were found as insufficient and 33 (66%) deficient in their Vitamin D status. In the moderate dry eye group, only 6 (12%) cases were found as insufficient in their Vitamin D status. In the mild dry eye group, only 1 (2%) case was found as insufficient and 3 (6%) cases were found to be normal in their Vitamin D status.

Table-IV

Association of vitamin D status with TBUT of Dry Eye Syndrome (DES) patients (n=50).

Vitamin D status (ng/mL)		TBU (sec)		p value
		< 10	>10	
Normal	>30	3 (6%)	0 (0%)	0.078ns
Insufficiency	20-29	14 (28%)	0 (0%)	<0.001s
Deficiency	<20	33 (66%)	0 (0%)	<0.001[s]

*Data were expressed as frequency and percentage
*Z-proportion test was performed to compare between the groups
*ns=not significant
*s= significant

In TBUT <10 sec group, 14 (28%) cases were found as insufficient, 33 (66%) cases were deficient and only 3 (6%) cases found as normal in their Vitamin D status. In TBUT >10 sec group, no cases were found as insufficient, deficient and normal in their Vitamin D status as all cases had dry eye. So, statistically significant differences were observed between the groups.

Table-V

Association of vitamin D status with Schirmer test 1 of Dry Eye Syndrome (DES) patients (n=50).

Vitamin D status (ng/mL)		Schirmer test 1 (mm/5 min)			
		Severe (0-4)	Moderate (5-9)	Mild (10-14)	Normal (≥15)
Normal	>30	0 (0%)	2 (4%)	1 (2%)	0 (0%)
Insufficiency	20-29	1 (2%)	9 (18%)	4 (8%)	0 (0%)
Deficiency	<20	5 (10%)	21 (42%)	7 (14%)	0 (0%)

*Data were expressed as frequency and percentage
*Schirmer test 1= Schirmer test without anesthesia

In the severe dry eye group, 1 (2%) case was found as insufficient, 5 (10%) cases were deficient in their Vitamin D status. In the moderate dry eye group, 9 (18%) cases were found as insufficient, 21 (42%) cases were deficient and only 2 (4%) cases were found as normal in their Vitamin D status. In the mild dry eye group, 4 (8%) cases were found as insufficient, 7 (14%) cases were deficient and only 1 (2%) case was found as normal in their Vitamin D status.

Table-VI

Association of vitamin D status with Schirmer test 2 of Dry Eye Syndrome (DES) patients (n=50).

Vitamin D status (ng/mL)		Schirmer test 2 (mm/5 min)			
		Severe (0-4)	Moderate (5-9)	Mild (10-14)	Normal (≥15)
Normal	>30	0 (0%)	2 (4%)	1 (2%)	0 (0%)
Insufficiency	20-29	0 (0%)	8 (16%)	6 (12%)	0 (0%)
Deficiency	<20	1 (2%)	24 (48%)	8 (16%)	0 (0%)

*Data were expressed as frequency and percentage
*Schirmer test 2= Schirmer test with anesthesia

In the severe dry eye group, 1 (2%) case was found as deficient in their Vitamin D status. In the moderate dry eye group, 8 (16%) cases were found as insufficient, 24 (48%) cases were deficient and only 2 (4%) cases were found as normal in their Vitamin D status. In the mild dry eye group, 6 (12%) cases were found as insufficient, 8 (16%) cases were deficient and only 1 (2%) case was found as normal in their Vitamin D status.

Table-VII

Correlation of vitamin D level with dry eye (n=50)

Variable		OSDI	TBUT	Schirmer test 1	Schirmer Test 2
Vitamin D	r value	-0.852	+0.479	+0.065	+0.320*
	p value	0.000s	0.000s	0.655ns	0.023s

*Pearson Correlation coefficient test was performed to observe the relation between dry eye and Vitamin D level.

In this study, dry eye was measured by OSDI, tear film breakup time (TBUT) and Schirmer test without and with anesthesia. Vitamin D level was positively correlated with TBUT, Schirmer test1 and Schirmer Test 2 and negatively correlated with OSDI. This correlation was statistically significant for TBUT, Schirmer Test 2 and OSDI.

Discussion

Vitamin D level can affect the immune system. Vitamin D strengthened the corneal epithelial barrier function through gap or tight junctions. It can control ocular surface inflammation by inhibiting Langerhans cell migration and corneal neovascularization. [6,10,11] Bae[12] reported that vitamin D supplementation is an effective and useful treatment for patients with DES. In the present study, dry eye was measured by OSDI score, tear film breakup time (TBUT), Schirmer test without and with anesthesia. OSDI score was found higher and fluorescein TBUT, Schirmer test without anesthesia and Schirmer test with anesthesia found lower score in dry eye patients. Almost similar study was found by different researchers of different countries. [2,8,13] But Jeon et al.[14] found no association between serum vitamin D levels and DES. Vitamin D level was positively correlated with TBUT, Schirmer Test 1 and Schirmer Test 2 and negatively correlated with OSDI in our study. This correlation was statistically significant for TBUT Schirmer Test 2 and OSDI. Yildirim et al. [1] and Jin et al. [2] agreed with our findings. They reported that tear break-up time (TBUT) and secretion were correlated with serum vitamin D levels. Vitamin D might be an important factor for dry eye syndrome. But Elagamy and Bawazir[15] and Arman et al. [16] demonstrated insignificant correlation with TBUT and Schirmer test.

Limitations

The limitation of our study was having small sample size and short study period in comparison to other studies. The effect of seasonal variation of vitamin D was not considered. Further study with a large sample size and longer study period is recommended.

Conclusions

After analyzing the results of the present study, it can be concluded that Vitamin-D deficiency appears to have an effect on ocular surface parameters in patients with dry eye syndrome. Therefore, vitamin D supplementation might be useful for mitigating the dry eye symptoms, including ocular discomfort, pain, redness, ocular fatigue, sensitivity to light and blurred vision.

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