

## The Evaluation of Mood Status in Dry Eye Patients

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### Abstract

**Aim:** To evaluate mood status in patients with dry eye syndrome (DES).

**Methods:** The study comprised of 78 eyes of 78 patients which were divided into two groups. Ocular surface disease index (OSDI), tear osmolarity, tear-film break-up time (TBUT), and Beck Depression Inventory - II (BDI - II) tests were used to assess the patients. All variables were compared within 2 groups.

**Results:** In patients with DES; the mean tear osmolarity, OSDI, and TBUT were  $315.9 \pm 14$  (306 - 346) mOsm/L,  $49.8 \pm 16.6$  (12 - 83), and  $4 \pm 1.2$  (2 - 8) sec respectively. In control group they were  $294.9 \pm 9$  (280 - 303) mOsm/L,  $8.5 \pm 5.5$  (0 - 11), and  $11.5 \pm 1.6$  (10 - 15) sec respectively ( $p = 0.001$ ). The BDI-II scores were  $18.3 \pm 14.3$  (4 - 74), and  $5 \pm 4.1$  (0 - 9) in two groups respectively ( $p = 0.001$ ).

**Conclusions:** This study demonstrated significant mood changes in patients with DES. Chronic ocular inflammation and irritation could alter the BDI - II score. Hence, negative mood status might be associated with an increase in ocular surface inflammation.

**Keywords:** Depression; Dry eye; OSDI; Tear film break-up time; Tear osmolarity

### Abbreviations

DES: Dry Eye Syndrome; DEWS: Dry Eye Work Shop; OSDI: Ocular Surface Disease Index; TBUT: Tear-Film Break-Up Time; BDI-II: Beck Depression Inventory - II; IL: Interleukin; TNF: Tumor Necrosis Factor

### Introduction

Dry eye syndrome (DES) is defined as a multifactorial disease of tear and ocular surface that results in symptoms of irritation, blurred vision and tear film instability due to increased tear osmolarity and inflammation [1,2]. Increased tear film osmolarity triggers the release of inflammatory substances which results in instability of the tear film and damage of surface epithelium. This imbalance of the ocular surface exacerbates the hyperosmolarity and activates the vicious cycle mechanism [2].

Symptoms seen in DES such as burning, stinging, itching, photophobia, tearing, and foreign body sensation generally affect the patients quality of life. The association between these two variables has been investigated in various studies [3-5]. In these studies, several

methods and techniques have been developed to quantify the impact of DES on various aspects of patient's mood and quality of life [3-5]. Although the exact pathogenic mechanism of association between DES and psychiatric disorders remains unclear, we postulate that the chronic discomfort seen in DES, has showed a negative impact on individual's mood and mental health [3]. Furthermore, negative mood status may increase ocular surface inflammation by some inflammatory agents which lead to the formation of a negative mood, and causes DES.

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Herein, the aim of this study was to evaluate the association between mood scores and the subjective and objective tests for the evaluation of DES.

### Materials and Methods

#### Study Population and Design

This study was conducted in compliance with the institutional and government review board regulations, informed consent regulations and the Declaration of Helsinki. Written informed consent was obtained from all patients.

Thirty-nine right eyes of 39 consecutive patients with DES who visited our dry eye clinic between June 2012 and June 2013, and willing to enroll in this study were participated and formed group 1. The diagnosis of DES was based on Dry Eye Workshop (DEWS) report [2]. Thirty-nine right eyes of age and sex matched subjects, applying for routine eye examination between the dates mentioned above, were enrolled in the study as the control group (group 2). Patients who had a history of ocular surgery, contact lens wearing during the previous 3 months, and the use of any psychiatric or systemic medications or artificial tears within 12 hours of checking tear osmolarity were excluded. We also excluded the patients having any ocular infection, allergy, punctal plugs, or any systemic diseases. Healthy subjects with symptoms of DES, or any other ocular or systemic diseases, and being under any medications were also excluded. Healthy subjects with symptoms of DES, or any other ocular or systemic diseases, and being under any medications were also excluded.

#### Examination Protocol and Measurements

After routine ophthalmologic examination including; visual acuity measurement, slit-lamp examination and intra ocular pressure measurement, all subjects underwent a complete evaluation of the ocular surface in the following order: dry eye symptom analysis with the ocular surface disease index (OSDI; Allergan, Inc, Irvine, CA, USA) scoring, measurement of the tear osmolarity with TearLab® Osmolarity System (TearLab Co., San Diego, CA, USA), and measurement of the tear-film break-up time (TBUT). A single examiner performed all these examinations (GDC).

The OSDI consists of 12 questions on symptoms within the past week and yields scores ranging from 0 (least severe) to 100 (most severe). A score of 12 was used as a cut-off for normal [6].

Subsequently, tear osmolarity was measured using a handheld TearLab® osmolarity device. The system was calibrated at the beginning of each study day with the same lot numbers as the test cards used for each tear osmolarity measurement. A 50 nL tear sample was

obtained from the inferior-lateral tear meniscus by the lateral canthus. A tear osmolarity value of 305 mOsm/L was used as the cut-off for dry eye [7].

The TBUT was measured by installing fluorescein 1% eyedrop into the inferior fornix. The interval between a complete blink and the appearance of the first dry spot was noted. The average of three consecutive TBUT measurements was taken. An average TBUT value less than 10 seconds was considered as abnormal [8].

Finally, the Beck Depression Inventory - II (BDI - II) test, a revision of the BDI, was used to measure the severity of mood in all subjects. The test contains 21 questions and examines emotional, behavioral, and somatic symptoms. Each answer was scored on a scale value of 0 to 3. The used cut-offs were as follows: 0 - 13: minimal depression; 14 - 19: mild depression; 20 - 28: moderate depression; and 29 - 63: severe depression, which were differed from the original BDI cut-offs. A persistent score of 17 or above indicates that the patient may need medical treatment for psychological support [9].

After a proper description of the OSDI and the BDI-II questionnaires to the subjects, it was expected to performed the tests themselves.

### Statistical Analysis

Statistical analysis was performed using SPSS ver. 20.0 (SPSS Inc., Chicago, IL, USA). The average OSDI, tear osmolarity, TBUT, BDI - II and demographical variables were compared among two groups using the Student t test, Mann Whitney U test. Then, the average BDI - II score was correleted with other parameters using Pearson correlation analysis. All standard deviation values were given with the average results. Results were considered as statistically significant if the *p* value was less than 0.05. Correlation coefficient (*r*) showed a strong association between variables if it was higher than 0.5.

## Results

### Demographic Characteristics

There were 33 female (84.6%) and 6 male (15.3%) in group 1, and 32 female (82.1%) and 7 male (17.9%) in group 2 (*p* = 0.53). The mean age in group 1 and 2 were 50.8 ± 13.3 (25 - 80) years and 52.4 ± 6.7 (30 - 70) years, respectively (*p* = 0.75).

### Results of Tear Function Tests

The mean OSDI scores were 49.8 ± 16.6 (12 - 83) and 8.5 ± 5.5 (0 - 11) in group 1 and group 2, respectively (*p* = 0.001). The mean tear osmolarity in group 1 and group 2 were 315.9 ± 14 (306 - 346) mOsm/L and 294.9 ± 9 (280 - 303) mOsm/L, respectively (*p* = 0.001). The mean TBUT was 4 ± 1.2 (2 - 8) seconds in group 1, and 11.5 ± 1.6 (10 - 15) seconds in group 2 (*p* = 0.001). Demographic data and tear function test results of group 1 and 2 are summarized in Table.

	Group	n	Mean	SD	Range	t-test
<b>Age</b>	Group 1	39	50.8	13.3	25-80	Sig
	Group 2	39	52.4	6.7	30-70	<i>p</i> = 0.41
<b>OSDI</b>	Group 1	39	49.8	16.6	12-83	Sig
	Group 2	39	8.5	5.5	0-11	<i>p</i> = 0.001*
<b>Tear Osmolarity (mOsm / L)</b>	Group 1	39	315.9	14	306-346	Sig
	Group 2	39	294.9	9	280-303	<i>p</i> = 0.001*

<b>TBUT (second)</b>	Group 1	39	4	1.2	2-8	Sig
	Group 2	39	11.5	1.6	10-15	$p = 0.001^*$
<b>BDI-II</b>	Group 1	39	18.3	14.3	4-74	Sig
	Group 2	39	5	4.1	0-9	$p = 0.001^*$

**Table:** The demographic data and the comparison of the test values in groups.

Group 1: patients with dry eye syndrome; Group 2: healthy subjects; OSDI: ocular surface disease index; TBUT: tear-film break-up time; BDI - II: Beck Depression Inventory - II; SD: standart deviation.

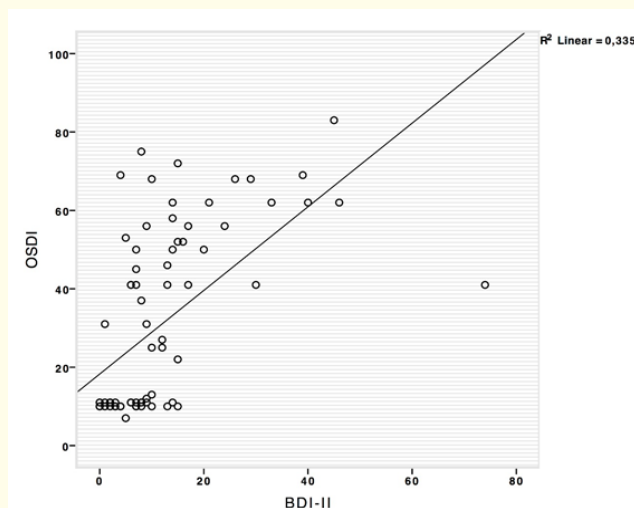
\* Indicate that the difference between the two groups was statistically significant for the t - test.

### Results of Beck Depression Inventory - II

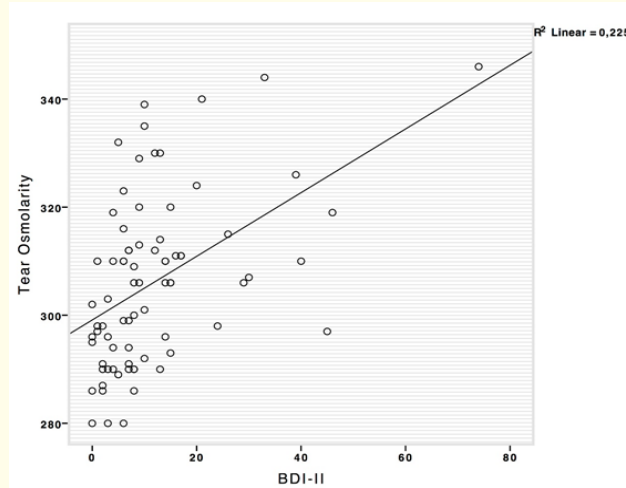
The mean BDI-II score in group 1 and group 2 were  $18.3 \pm 14.3$  (4 - 74) and  $5 \pm 4.1$  (0 - 9), respectively ( $p = 0.001$ ), (Table).

### Correlation Analysis

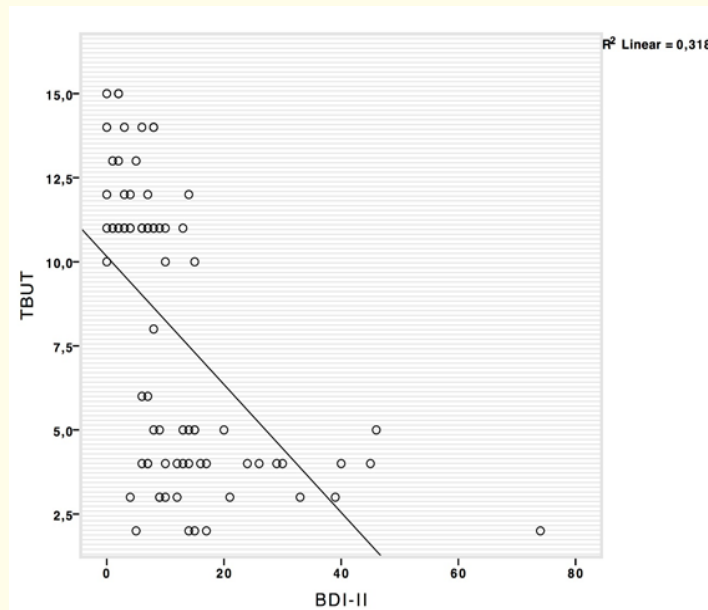
Correlation analysis revealed a significantly strong association between BDI - II scores and tear function tests for all subjects. The correlation coefficient was 0.579 ( $p < 0.001$ ) for BDI - II and OSDI, was - 0.564 ( $p < 0.001$ ) for BDI - II and TBUT, and was 0.474 ( $p < 0.001$ ) for BDI - II and tear osmolarity. Figures 1-3 show scatter plot graphics of BDI-II scoring against tear function tests for all subjects. Figure 1 shows the linear positive correlation between BDI - II scoring and OSDI ( $r = 0.579, p < 0.001$ ), Figure 2 shows the linear negative correlation of the BDI - II scoring and TBUT ( $r = - 0.564, p < 0.001$ ), and Figure 3 shows the linear positive correlation between BDI - II scoring and tear osmolarity ( $r = 0.474, p < 0.001$ ), respectively. After stratifying the groups, correlation analysis showed an unsignificantly positive correlation between BDI - II scoring and OSDI in group 1 ( $r = 0.293, p = 0.07$ ). However, there was not such an positive correlation between BDI - II scoring and OSDI in group 2 ( $r = - 0.138, p = 0.40$ ). Interestingly, it was found that there was a positive correlation between age and BDI - II scoring in group 1, but not in group 2 ( $r = 0.340, p = 0.03; r = 0.122, p = 0.45$ , respectively).



**Figure 1:** Scatter plots of BDI - II scoring against OSDI for all subjects. The correlation coefficient for this association was 0.579 ( $p < 0.001$ ).



**Figure 2:** Scatter plots of BDI - II scoring against TBUT for all subjects. Linear negative correlation revealed a correlation coefficient of -0.564 ( $p < 0.001$ ).



**Figure 3:** Scatter plots for the association between BDI - II scoring and tear osmolarity. The correlation coefficient for this linear positive correlation was 0.474 ( $p < 0.001$ ).

### Discussion

In this study, we aimed to identify the association between the mood status and DES, and our results revealed that depressive mood status was closely related to the signs of DES. It is also surprising that the results revealed a positive correlation between the BDI - II scor-

ring and age in group 1 however; a similar correlation was not found between the BDI - II scoring and age in group 2. So, we advocated that increasing age and chronic ocular inflammation and irritation could alter the BDI - II scoring in dry eye patients.

Dry eye syndrome is a growing public health problem, which negatively impacts the individual's physical, social, psychological functioning, daily activities, workplace productivity and quality of life by causing visual impairment and fatigue [3]. Besides the negative effects on the visual acuity, vision-related quality of daily life, and overall health, it has an unproportional relationship among the clinical findings and symptoms. Thus, etiology and symptoms of DES have various presentations [4,5]. Therefore, it would be more appropriate to make an symptom based assessment when evaluating a patient who has mild-to-moderate DES [2,10].

There are still many ongoing questionnaires for DES which are studied to determine the most accurate and reliable questioning in repeated assessments [3,11]. To evaluate the dry eye symptoms, the most commonly used survey is OSDI, which was developed by the Outcomes Research Group [12,13]. It assesses the relationship between environmental factors and the individual's symptoms and its' impact on visual function and daily life [14]. Besides helping to make the diagnosis, it provides assessment of the severity of the symptoms [14].

Similar to the OSDI, we used a validated questionnaire for assessing the mood status in all subjects. The BDI - II, a 1996 revision of the BDI, consists of 21 groups of statements which describe the way patient have been feeling during the past 2 weeks, including the test day. The revision involves the following items; change in the image of the body, hypochondriasis, difficulty working, sleep loss and appetite loss, and the standardized cut-offs were used to differ it from the original BDI. Higher total scores indicate more severe depressive symptoms. Also, a consistent score of 17 and above indicates that the patients need medical treatment. Scores can be exaggerated or minimized by the subject like the other self-administered questionnaires. Nevertheless, it has been used by psychiatrists, health care providers, or the doctors other than psychiatrists to rich a quick diagnosis [9].

Previous studies have reported that dry eye symptoms usually occur before the clinical signs of the disease, and there is no correlation between the subjective symptoms and ocular signs in patients with DES [10]. This unproportional relationship may be related to the downregulation of corneal sensitivity by the chronic stimulation of corneal neural axis in DES [14,15]. Moreover, individual pain detection threshold and psychosocial conditions can affect the severity of ocular symptoms [16,17].

Several studies investigated the effects of age, sex, and drugs on DES and low mood status [18-21]. It remains obscure whether DES affects the mood status negatively, or negative mood status enhances the feeling of discomfort in patients with DES. On the other hand, chronic DES remains unresponsive to medical therapy, and this condition may facilitate the negative feelings [22].

In this study we showed that there is a positive correlation between DES and low mood status. This result is comperable with the other studies investigating the relationship between DES and depression [15,16]. But, in our study patients do not have the diagnosis of any psychiatric disorders such as depression, posttraumatic stress disorder, or others. Actually, we assessed the prevalence of low mood condition in patient group with DES in our clinic. It was surprising that a high amount of dry eye patients have elevated scores of BDI - II scoring. Additionally, BDI - II scores elevated with the increased patient age in DES patients, however, in healthy subjects age did not affect the test scoring. So, it can be interpretable that mood status can be altered more negatively in elder dry eye patients.

Recently, the increase in tear osmolarity and inflammation has been suggested as the main triggering mechanism in DES [2]. If inflammation is believed to be the main factor, the presence of an inflammatory precursor, which is underlying the DES and low mood status, should be investigated. N - 6 and n - 3 , poly unsaturated fatty acids are essential for human health and have anti-inflammatory properties. Researches have indicated that the elevated levels of n - 6 : n - 3 affects the level of interleukin (IL) - 1, IL - 6, and tumor necrosis factor (TNF) -  $\alpha$ . These cytokines not only trigger the inflammation cascade on the ocular surface, but also lead to the formation of a negative mood by neurotransmitter discharge and signal transmission [23-26]. Miljanovic, *et al.* have revealed that there is a positive correlation

between the high n - 6: n - 3 and DES [23]. In addition, patients with depression may have a lower threshold for physical discomfort or pain perception. Kwon, *et al.* demonstrated that poor treatment outcomes, physical disability and potentially resulting in early mortality due to lower pain threshold in patients with chronic prostatitis, pelvic pain syndrome and depression [27]. In consideration of these results from previous studies, we speculated that patients with low mood status, may show extreme sensitivity to initial level of dryness or demonstrate an incompatible clinical symptoms with the disease severity.

There are several limitations of our study. First, we did not exclude the female subjects in menopausal age although we know that DES and low mood status might have been developed due to the fluctuations in sex hormones with menopause [18,28]. Nevertheless, it might not significantly affect the results due to the mean age and gender between the two groups were stratified. The second limitation is that none of the patients had an existing mood disorder diagnosed by psychiatrist. However, these patients were referred to the department of psychiatry for the exact diagnosis. Additionally, the OSDI and the BDI - II questionnaires were completed by self administration, and this condition might have an impact on the final score.

In conclusion, this study revealed that DES patients have significantly low mood status compared to the healthy subjects. If this interpretation is correct, it is necessary to consult a patient with DES to a psychiatrist routinely. Prospective multidisciplinary studies considering the negative impact of the self administration, age, and the hormonal status, which are the limitations of this study, are needed to understand the main association between DES and low mood status.

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