



Comparison of OSDI Score & Conjunctival Ultraviolet Autofluorescence in Normals and Dry Eye Patients

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Abstract

Purpose: We investigated the association between ocular surface disease index (OSDI) score and conjunctival ultraviolet autofluorescence (CUVAF) in normals and dry eye patients.

Methods: Subjects aged 18 to 65 years were enrolled after obtaining a written informed consent and a comprehensive ocular evaluation. Dry eye diagnosis was made objectively using Tear film break-up time and Schirmer's 1 test. OSDI questionnaire were used to assess the symptoms of dry eye. Sun exposure was assessed using Melbourne visual impairment questionnaire. UV induced conjunctival damage was measured using CUVAF photography which consist of custom developed smartphone-based camera system. Setup includes a portable eye cup placed on smart phone camera fitted with UV emitting LED. Autofluorescence photographs of the nasal and temporal conjunctiva were captured. The conjunctival area of damage identified using CUVAF photography was outlined traced using polygon selection tool in ImageJ software and area was calculated.

Result: Mean age of subjects in normal group (N-30) was 23.4 ± 6.37 and dry eye group (N-30) was 30.83 ± 13.75 . Mean OSDI score in dry eye group was of 27.37 ± 10.42 which was significantly higher ($p < 0.05$) compared to normal group 9.59 ± 9.19 . The average TBUT score in normal group was 11.56 ± 1.99 , and in dry eye group was 4.83 ± 2.789 with significant difference ($p < 0.05$). Mean conjunctival area of damages in right and left eye of normal group was 2234.1 ± 4891.4 and 1498.8 ± 4130.5 with no significant difference ($p > 0.05$). Similarly, in dry eye group was 4828.43 ± 5805.5 and 4755.88 ± 5514.8 with no statistically different ($p > 0.05$). Average CUVAF area showed a weak negative correlation with OSDI score ($r = -0.48$) ($p > 0.05$).

Conclusion: CUVAF is a valuable tool to assess UV induced conjunctival damage. CUVAF area was significantly higher in dry eye group than normals. Average CUVAF area was negatively correlated with subjective symptoms of dry.

Keywords: Dry Eye; OSDI; Conjunctival Ultraviolet Autofluorescence; CUVAF; Sun Exposure; UV Exposure; Teal Film

Abbreviations

DED: Dry Eye Disease; UV: Ultraviolet; CUVAF: Conjunctival Ultraviolet Autofluorescence; UVAF: Ultraviolet Autofluorescence; TBUT: Tear film Break Up Time; OSDI: Ocular Surface Disease Index.

Introduction

Dry Eye Disease (DED) is common ocular surface disorder with prevalence 5-50% of world's population [1]. DED is characterized by instability of the tear film that results in ocular discomfort and visual disturbance. Sun exposure is a modifiable risk factor for diseases like pterygium & pinguecula [2]. Recent studies have suggested that greater time spent outdoors is positively correlated with prevalence of DED [3,4]. Due to excessive exposure to the harmful effects of ultraviolet (UV) rays from the sun, tear film may evaporate from the ocular surface more quickly, leading to the symptoms of DED. Conjunctival Ultraviolet Autofluorescence (CUVAF) is a method of detecting conjunctival damage due to sun exposure [5,6]. CUVAF areas is obtained from ultraviolet autofluorescence (UVAF) photography [6,7]. There is a significant correlation between sun exposure and DED. Similarly, CUVAF area is significantly correlates with level of outdoor activity [7,8]. But there is a lack of knowledge about the relationship between DED and CUVAF which is yet to be explored. Hence, the aim of our study was to investigate the relationship between OSDI score and CUVAF in subjects with and without DED.

Materials and Methods

A prospective, observational, cross-sectional study was held at the department of Optometry, SRM Medical College Hospital and Research Centre, Chennai with approval of the institutional ethics committee and considering the tenets of the Declaration of Helsinki. Participant who satisfies the inclusion criteria were included in the study after a detailed explanation about the study and obtaining informed consent form the participant. Subjects were recruited in the study through convenient sampling technique and subjects were screened on the basis of subjective symptoms and clinical test for DED. On the basis of screening subjects were classified into two groups, group 1 as normals with no subjective symptoms and negative dry eye clinical test and group 2 as dry eye with positive OSDI score and positive TBUT test [9]. Participants aged 18 to 65 years with and without dry eye was included in the study. Participants with any extensive ocular pathologies and infections, participants undergone any ocular surgery, pregnancy and lactation were excluded after a detailed history taking and comprehensive ocular examination.

Questionnaires

OSDI questionnaire were used to assess the symptoms of DED and its effects on vision in the previous two weeks of patient's life [10]. It consists of 12 questions with three domains. Participants response was rated on a scale of 0 to 4, with 0- none of the time, 1- some of the time, 2 - half of the time, 3 - most of the time and 4 - all of the time. Overall OSDI score ranges between 0 - 100 which is classified based on the severity of the symptoms. Normal OSDI score ranges from 0 - 12. UV exposure in all subjects were assessed using 'Melbourne visual impairment questionnaire' which collects the details regarding the duration and frequency of sun exposure from birth [11,12]. The questionnaire also collects details regarding the use of ocular protective aids like spectacles, sunglasses and hat or turbans while involving in outdoor activity and the frequency was marked on a 1 to 5 scale where '1' refers to never, '2' refers to less than half of the time, '3' refers to half of the time, '4' refers to more than half of the time and '5' refers to all of the time and used for analysis as numbers which indicate '0' as never, '0.25' as seldom, '0.50' as half time, '0.75' as usually, '1.00' as always.

Clinical DED Evaluation

Clinical diagnosis of DED was done using TBUT and Schirmer's 1 test. To measure TBUT, fluorescein was instilled into the patient's tear film and tear film was observed under cobalt blue illumination in slit lamp. The TBUT value is recorded as the number of seconds that taken for the appearance of the first dry spot in the tear film. Normal TBUT value is >10 seconds. Schirmer's test was done by placing a no. 41 Whatman filter paper which is 5×35 mm in the inferior temporal side of conjunctival sac. The strip is removed after 5 minutes and the wetting of tears is measured in millimetres. Value >15 mm in 5 minutes refers to normal.

Conjunctival Ultraviolet Autofluorescence

UV induced conjunctival damage was captured using a custom-made portable device (Figure 1). Setup include a portable eye cup placed on iPhone camera fitted with four ultra-bright deep violet LED (<https://www.thorlabs.com/>) with transmittance range 300 to 400 nm and peak 375 nm wavelength which is placed adjacent sides of eye cup (Figure 2). An additional two white light LED was placed on alternate side for focusing the eye. The basic principle of the set up include UV LED will emit UV and camera captures the autofluorescence. Damaged conjunctival area will be appeared as patchy white colour (Figure 3). CUVAF images were captured in a dim illuminated room and normal eye photographs were captured with white LED.



Figure 1: Shows custom developed smartphone-based conjunctival ultraviolet autofluorescence photography system used to measure the conjunctival damage.

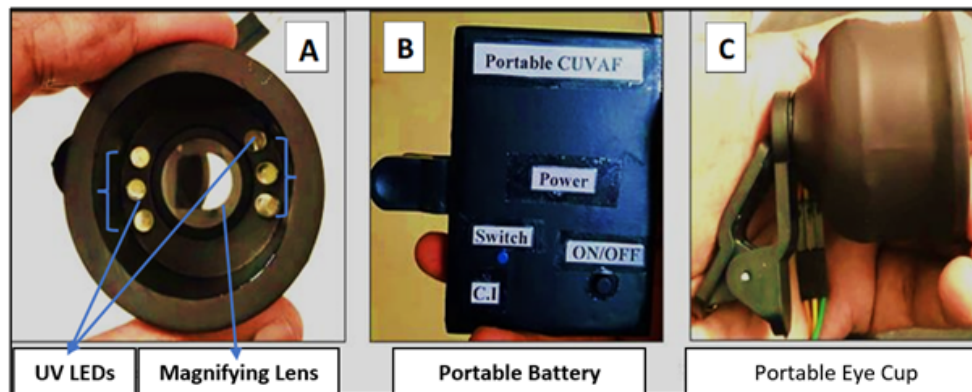


Figure 2: A: Shows ultra-bright deep violet LED with transmittance range 300 to 400 nm and peak 375 nm wavelengths which are placed adjacent sides of the eye cup with magnifying lens at the centre. B: Shows portable rechargeable battery attached with a micro clip that can be fit to any smartphone device. C: Shows, eye cup fixed on a micro clip which can be attached on the smart phone back camera.

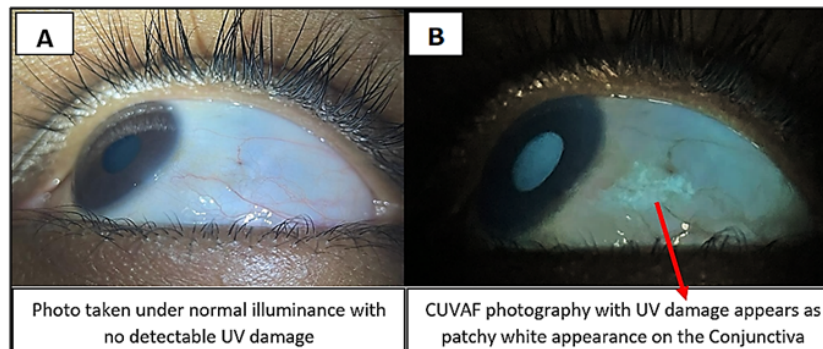


Figure 3: A: Shows the picture of temporal conjunctiva of subject taken under normal illumination; B: Shows the picture of temporal conjunctiva of same subject taken using CUVAF photography system, where UV damage appears as patchy white colour on the conjunctiva.

The image analysis was done using ImageJ software (<https://imagej.nih.gov/ij/download.html>). The area of damage was outline traced using polygon selection tool in ImageJ software (Figure 4) and area in mm² were calculated. The nasal and temporal regions of each eye was measured and the average obtained was used in statistical analyses.

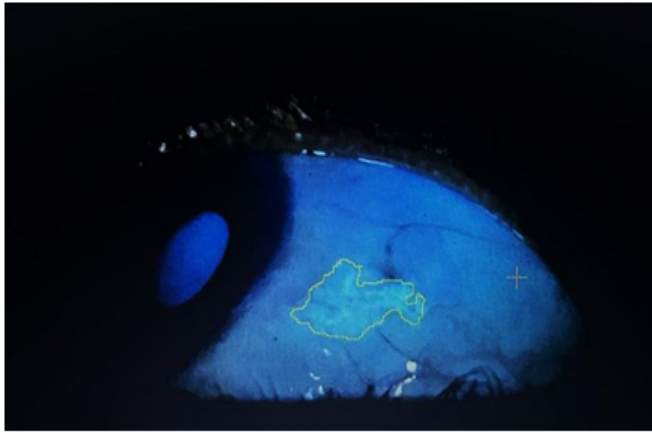


Figure 4: Shows area of conjunctival UV damage outlined using polygon selection tool in ImageJ software.

Statistical Analysis

Quantitative variables were expressed as mean and standard deviation. Kolmogorov-Smirnov test was used to check the normality of distribution. Paired T test and Independent T test were used to compare mean values. Correlation analysis was done using Pearson's correlation coefficient. The scatterplot was used to visualize the correlation data.

Results and Discussion

Results

Demographic Details: Sixty participants were included in the study of which 30 (50%) were normal, 30 (50%) had dry eye. Of the 60 participants 25 (41.6%) males and 35 (58.3%) females and the mean \pm SD age (years) of subjects in normal group was 23.4 ± 6.37 (N- 30) and dry eye was 30.83 ± 13.75 (N- 30).

Subjective Symptoms: Dry eye symptoms were in the moderate range in dry eye group with a mean \pm SD of 27.37 ± 10.42 which was significantly higher ($p=0.049$) compared to normal group 9.59 ± 9.19 . OSDI subscale score result shows that, in each three domain the score was significantly higher in dry group compared to normal ($p < 0.05$).

Clinical Test: The average TBUT score (seconds) in normal group was 11.56 ± 1.99 , while the average TBUT among the dry eye group was 4.83 ± 2.789 with significant difference ($p = 0.018$). Similarly, the average Schirmer's score (mm) in normals and dry eyes group was 28 ± 6.34 and 23.53 ± 9.55 respectively, with no significant difference ($p = 0.95$).

Conjunctival Ultraviolet Autofluorescence (CUVAF):

While comparing the temporal and nasal area of conjunctival damage in both eyes showed no significant difference ($p = 0.68$). The average value of temporal and nasal area was taken for analysis. Figure 5 shows, the mean conjunctival area of damages (mm²) in right and left eye of normal group was 2234.1 ± 4891.4 and 1498.8 ± 4130.5 with no significant difference ($p = 0.09$). Similarly, in dry eye group was 4828.43 ± 5805.5 and 4755.88 ± 5514.8 respectively. However, this difference was not statistically different ($p = 0.095$).

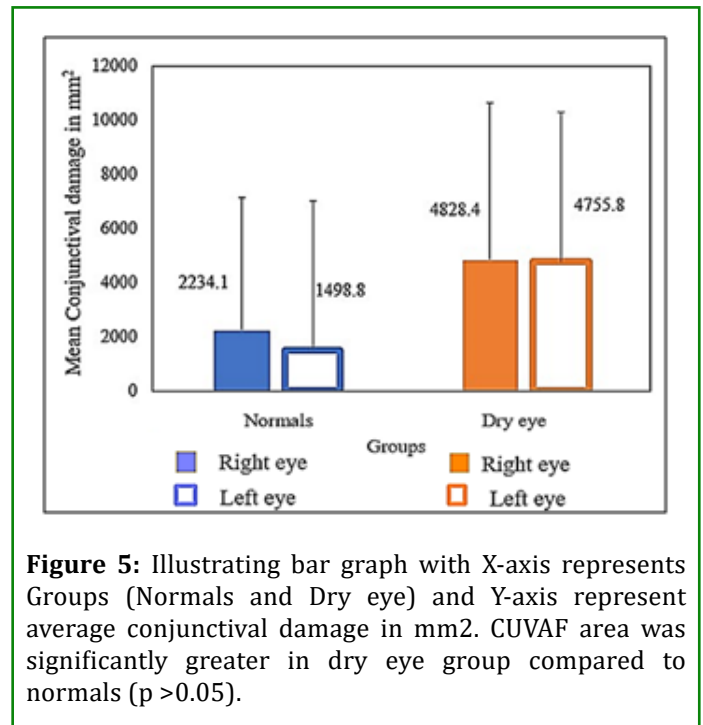


Figure 5: Illustrating bar graph with X-axis represents Groups (Normals and Dry eye) and Y-axis represent average conjunctival damage in mm². CUVAF area was significantly greater in dry eye group compared to normals ($p > 0.05$).

Correlation between CUVAF Characteristics and Subjective Symptoms of Dry Eye:

The OSDI score showed a weak negative correlation with CUVAF area of damage in normals and dry eye group ($r = -0.48, -0.16$) with no significant difference ($p = 0.3, 0.8$). Similarly, CUVAF pixel intensity showed a weak negative correlation with OSDI score in normals and dry eye group ($r = -0.32, -0.38$) with significant difference ($p < 0.05$) (Figure 6).

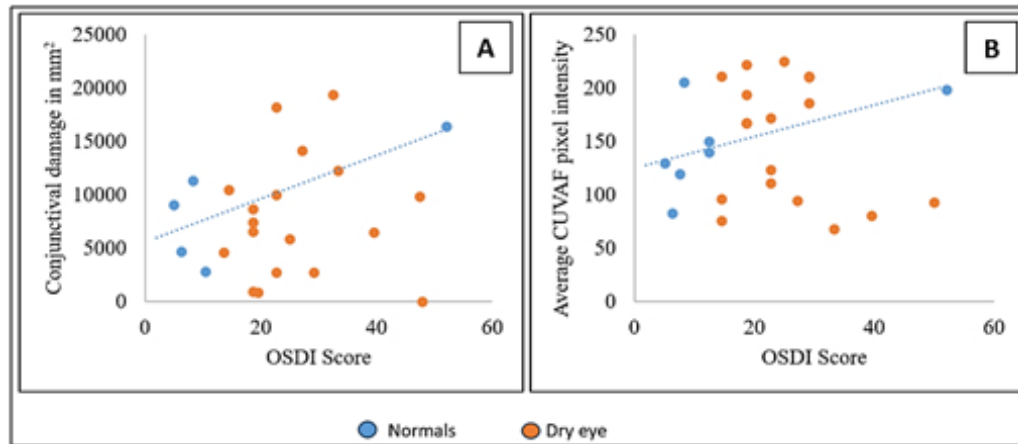


Figure 6: A: Illustrate scatter plot with X-axis represents OSDI score and Y-axis represents average conjunctival damage in mm². OSDI score showed a weak negative correlation with CUVAF area of damage in normals and dry eye group ($r = -0.48, -0.16$), ($p > 0.05$).

B: Illustrate scatter plot with X-axis represents OSDI score and Y-axis represents average CUVAF pixel intensity. CUVAF pixel intensity showed a weak negative correlation with OSDI score in normals and dry eye group ($r = -0.32, -0.38$), ($p < 0.05$).

Correlation between CUVAF Characteristics and Clinical Test for Dry Eye: The average TBUT score showed a weak positive correlation with CUVAF area of damage in dry eye group with significant difference ($r = 0.41$), ($p = 0.02$). But in

normal group shows a weak negative correlation with CUVAF area of damage and TBUT with no significant difference ($r = -0.06$), ($p = 0.9$) (Table 1).

	n/60	Average Area of CUVAF (mm) ²		Average CUVAF Pixel Intensity	
		r	p	r	p
TBUT					
Dry eye	30	0.41	0.02	0.27	0.13
Non-Dry eye	30	-0.06	0.92	0.02	0.89
Schirmer's test					
Dry eye	25	0.07	0.703	0.12	0.51
Non-Dry eye	35	0.27	0.14	0.3	0.1

(n/60 - number of responses in each category out of 60).

Table 1: Shows the correlation between average area of CUVAF damage, average CUVAF pixel intensity and dry eye test parameters (TBUT, Schirmer's) in normal and dry eye group.

Life Time Ocular Sun Exposure (OE eff): The average OE eff in normal subjects was 4295 ± 3069 and in dry eyes group was 4442 ± 4652 , with no significant difference ($p = 0.88$). The information regarding the use of sun protective aids in normals and dry eye group. In dry eye group, 10 people were using spectacle all of the time while going out, 4 people was using sunglasses less than half of the time and 6 people were using hat/ helmet more than half of the time while going out. 11 people have sun gazing habit which was less than 10 minutes per day. The number of migrations was < 1 in majority of the participants.

Receiver Operating Characteristics (ROC) Curve for CUVAF: The area under the Receiver operative curve (AUC) for CUVAF was 0.672 (95 % CI: 0.533 - 0.811), ($p = 0.02$) which was acceptable.

Discussion

Dry eye is common ocular surface disorder with increased prevalence worldwide. Since it is a multifactorial disorder, environmental factors like increased outdoor activities and UVR exposure may play a major role. The main aim of

our prospective observational cross-sectional study was to investigate whether excessive UVR exposure could create a positive impact against the development of DED and to identify the correlation between subjective symptoms of DED assessed using OSDI questionnaire and CUVAF in normal healthy patients and dry eye patients. To the best of our knowledge this is the first study to investigate the correlation between CUVAF and dry eye in India. CUVAF is a validated tool to assess UV induced conjunctival damage. The major highlight of the study was developing a smart phone based portable device which is capable of detecting UV induced conjunctival damage before the clinical manifestation of ocular symptoms. The instrument consists of a smartphone camera with good quality and UV LED with wavelength 300 - 4000 nm wavelength and peak 375 nm, which will emit UV and the camera, captures the autofluorescence.

The result from current study indicates that the subjective symptoms were in moderate range in dry eye patients and the OSDI score was significantly high in dry eye group compared to normals. Similarly, the clinical evaluation of DED with TBUT test and Schirmer's test was higher in dry eye patients compared to normals, which supports the study reported by Unlu, et al. [13]. We also found out, dry eye patients have higher CUVAF area of damage compared to the normal group and the region of CUVAF damage was different in both the groups. We observed a weak negative correlation between the subjective symptoms of DED with CUVAF area of damage and average pixel intensity in both the study group which was previously reported by Kearney, et al. [14] but we found a weak positive correlation between clinical tests of DED and CUVAF in dry eye patients which is different from the study reported by Kearney, et al. [14] this difference may be due to change in climatic condition between the two study regions.

Previously multiple authors have reported that Conjunctival damage was more on nasal conjunctiva than temporal conjunctiva due to peripheral light focusing effect (PLF), but current study did not show any evidence of more nasal conjunctival associations in contrast with other studies Kearney, et al. [15-17]. Melbourne visual impairment questionnaire was used to assess the Lifetime ocular UVR exposure which will collect details of sun exposure from birth. In current study, out of 60 participants, 30% were spectacle users and 10% were a sunglass user which was less than half of the time while going out. 16% of participants were using hat when they are engaged in outdoor work. 45% subjects were having sun gazing habit which was less than 10 minutes per day. 95% of the subjects have migration less than 1 and 5% of participants have more than 1 migration. The average lifetime ocular UVR exposure was slightly more in dry eye group compared to normal group but this difference was not statistically significant since majority of the subjects were engaged in same kind of outdoor activities

and UVR exposure.

In current study, there was homogeneity in age of study population, since, age is a factor affecting sun exposure, as age increases the CUVAF also increases. About 90% of UV exposure happens in age less than 18 years. The study also found out CUVAF can be used as a tool for diagnosis of DED. The ROC Curve was used to assess the sensitivity and specificity of CUVAF as a diagnostic test for dry eye. The area under the curve in ROC measures the precision of the test to correctly diagnose the disease. The AUC for CUVAF was 0.672 which come under good accuracy, which is not yet reported in any studies. The major limitations of the study were difficulty to identify conjunctival damage with poor quality images. The recall bias was a major drawback with the sun exposure questionnaire because it collects information regarding sun exposure from birth. Participant involved in more than two outdoor works; the prominent outdoor activity was only taken for analysis [18].

Conclusion

Dry eye is a multifactorial disorder of ocular surface. Excessive UV exposure is one of the major preventable risk factors of DED. CUVAF is a valuable tool to assess pre-clinical sun light induced ocular diseases like pterygium and pinguecula. The current study reported that CUVAF area was significantly higher in dry eye patients and average CUVAF area was negatively correlated with symptoms of DED. CUVAF plays an important role in screening UV induced ocular diseases which will help to avoid vision related and ocular health complications. The major advantage of the study was developing a smart phone based portable device which can be attached to any smartphone with good camera clarity which can be easily used in any clinical setup for early detection and prevention of UV induced conjunctival damage. It can be also helpful full in future studies concentrating of UV and ocular effects.

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Disclaimer

The authors report no conflicts of interest and have no proprietary interest in any of the materials mentioned in this article.

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