Diagnosis of Dry Eye Syndrome Using Ocular Surface Disease Index, Tear Film Break-up Time, and Schirmer Test

Sadia Humayun¹, Muqaddas Noor², Muhammad Shahid¹, Syed Abid Hussain Naqvi³, Mazhar Ishaq³ and Quratulain Humayun⁴

¹Refractive Surgical Department, Armed Forces Institute of Ophthalmology (AFIO), National University of Medical Sciences, Rawalpindi, Pakistan
²Eye Department, CMH Quetta, Pakistan
³Eye Department, Mazhar Ishaq Centre of Ophthalmology, Rawalpindi, Pakistan
⁴Child and Family Asthma Studies Centre, Women and Children Hospital, Buffalo, New York, USA

ABSTRACT
Objective: To evaluate the subjects of possible ocular surface dysfunction in dry eye syndrome (DES) by using Ocular Surface Disease Index (OSDI) questionnaire and correlating it with the tear film break-up time (TBUT) test and Schirmer test.
Study Design: Cross-sectional, observational study.
Place and Duration of the Study: Armed Forces Institute of Ophthalmology (AFIO), National University of Medical Sciences (NUMS), Rawalpindi, Pakistan, from March to August 2022.
Methodology: Demographics and detailed ophthalmological examinations were carried out for all the patients using slit lamp biomicroscopy. The questionnaire for OSDI was filled to calculate the OSDI score, Schirmer test, and TBUT test were performed for all patients. For statistical analysis, the mean test score of both eyes was used. Correlations between tests were drawn and reported.
Results: This study was conducted on ninety-seven adult participants with mean age of 31.3 ± 10.7 years, comprising of forty-five (46.4%) females and fifty-two (53.6%) males. The mean score for OSDI, TBUT, and Schirmer test was found to be 16.03 ± 14.22 (range 0 – 62.5), 9.63 ± 4.54 seconds (range 2.5 – 22.5), and 24.6 ± 10.85 mm (range 4.5 – 35.5), respectively. An inverse correlation was found between the OSDI and Schirmer, and OSDI and TBUT test scores which was also statistically significant. Schirmer and TBUT test scores also showed significant correlation.
Conclusion: The OSDI is quick, precise, feasible for self-assessment, and non-invasive standardised tool for evaluating symptoms of dry eye disease, hence it can aid in the diagnosis of DES.

Key Words: Dry eye syndrome, Ocular surface, Tear film break-up time, Schirmer test.

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INTRODUCTION

Dry eye syndrome (DES) is a complex clinicopathological entity and heterogeneous group of conditions characterised by hyperosmolarity and tear film instability over ocular surface caused by inadequate production or excessive evaporation. Various symptoms are caused by DES that can affect quality of life as well as work productivity.

Estimated burden of DES in Pakistani population is 18.7% and is reported to be 11.59% globally. However, there is considerable difficulty in the clinical diagnosis of dry eyes owing to discordance between the clinical signs and patients' reported symptoms.

The significant risk factors related with dry eyes are old age, female gender, contact lens usage, history of ocular or laser refractive surgery, blink disorders, disorders of eye-lids, and presence of concurrent ocular surface disorder. DES also have an association with systemic diseases like, Sjogren’s syndrome, rheumatoid arthritis, gout, thyroid disease, Stevens Johnson’s syndrome, asthma, and autoimmune disorders. In addition to that, there are some environmental factors that can trigger DES including low room humidity, high temperature, indoor/outdoor air pollution, and certain lighting conditions.

Allergen Outcome Research Group developed Ocular Surface Disease Index (OSDI), which is the most authentic question-
naire. This 12-item questionnaire provided symptom based assessment of dry eyes and its impact on visual function. DES can be diagnosed by various other tests and non-invasive instruments. Most preferable diagnostic tests are; tear film break-up time (TBUT), Schirmer test, staining of ocular surface with fluorescein sodium, lissamine green, and rose bengal. Some of the quantitative but high priced diagnostic tests include tear film osmolarity, lactoferrin levels, micro assays of immunoglobulin E (IgE), matrix metalloproteinase 9 (MMP-9), interferometry, and infrared meibography. The estimation of blink rate is also very crucial.

The aim of this study was to evaluate the subjects of possible ocular surface dysfunction by using OSDI and correlating it with tear film break up time (TBUT) test and Schirmer test.

**METHODOLOGY**

This cross-sectional, observational study was carried out at the Armed Forces Institute of Ophthalmology, between March to August 2022. Institutional Ethical Committee’s approval was obtained, and informed consent was taken from all subjects. Demographic data and past medical, and ocular history were recorded. The exclusion criteria were patients of DES, previous intra-ocular surgery, any ocular or systemic disease associated with DES, and topical or systemic drugs (benzodiazepines, anti-histamines, B-blockers etc.) that could cause DES. To determine whether the correlation coefficient differed from zero, the sample size was calculated by means of UCSF clinical and translational science institute sample size calculator using the following formula: \[ N = \frac{[(Z_{a} + Z_{b})/C]^2 + 3}{0.5 \times \ln[(1+r)/(1-r)]] \].

The standard normal deviate for \( \alpha = Z_{a} = 1.9600 \). The standard normal deviate for \( \beta = Z_{b} = 0.8416 \). A two-tailed hypothesis with 95% confidence interval, a power of 80% and an expected correlation of at least 0.3 yielded a sample size of 85. Adjusting for 10% attrition rate, the final sample size was 94.

OSDI is a validated questionnaire, consisting of 12 questions on account of reliability and validity of data from subjects. It was divided into three groups. Questions regarding ocular symptoms were presented to the first group, second group contained questions related to ocular symptoms while reading a book or watching television. Third group questions inquired about symptoms caused by the environmental factors. It scored as 0 to 4 where 0 depicted none of the time; score 1 depicted symptoms some of the time, score 2 corresponded to half of the time, score 3 showed most of the time, and 4 corresponded to all of the time. Total scoring of OSDI was calculated by the formula:

\[ \text{OSDI} = (\text{sum of score of all answered question}) \times 25 \div \text{total questions answered.} \]

Disease severity was assessed into four categories: normal, mild, moderate, and severe. A score \( \leq 12 \) was considered normal, >12 to <22 as mild dry eyes, 23 to 32 as moderate, and >32 score as severe dry eye disease. Furthermore, for analysis, all patients were divided into 3 groups according to their OSDI scores. Group 1 had normal and mild OSDI score (0 to <22 points), Group 2 had moderate OSDI score (23–32 points), and Group 3 had severe/high OSDI score (32–100 points). Any significant difference between the two tests scores in the groups was analysed.

Detail ophthalmological examination was carried out for each patient consisting of corrected distance visual acuity (CDVA), IOP measurement using non-contact tonometer, anterior and posterior segment examination using slit lamp biomicroscopy. The OSDI questionnaire was then filled by all participants to calculate the OSDI score. Schirmer test and TPUT test were performed after the routine ophthalmological examination and OSDI scoring.

For assessment of reflex and basal tear secretions, Schirmer I test was performed without anaesthesia. Any manipulation of eye before the test was avoided. To estimate the quantity of tears secreted, rounded end of 35x5 mm Schirmer tear strips (Ref no. MIPL/BOX/A1/01) were inserted into the inferior lateral cul-de-sac while patient looked up. Patients were instructed to look straight in front and blink normally for five minutes. Strip was then removed and length of wet filter paper was measured. For statistical analysis, the mean test score of both eyes was used. The cut-off value of Schirmer I test for dry eye disease was ≤10 mm/5 minutes.

TBUT was performed to check stability of tear film. A single drop of 0.5% Proparacaine Hydrochloride solution (Alcon Laboratories) was instilled in conjunctival sac. Sterile fluorescein sodium ophthalmic strip was placed in the lateral fornix for few seconds. Patients were advised to blink few times so that fluorescein was mixed with tear film, and then directed not to blink at all and to keep the eyes open. Under slit lamp biomicroscope with cobalt-blue filtered light, the tear film was examined and with the help of a stopwatch, the time elapsing between the last blink and formation of first dry spot (i.e break in tear film) was recorded. The same process was repeated three times. Mean TBUT score of right eye was calculated by taking the average of three readings. Same steps were repeated for the left eye. For statistical analysis, the mean TBUT score of both eyes was used. A TBUT of <10 seconds was taken as abnormal.

For statistical analysis, IBM SPSS (version 21.0) was used. The categorical variables were expressed as counts and percentages, and continuous variables were expressed as mean and SD. The correlation analysis was performed between the OSDI, TBUT and Schirmer test scores. Pearson correlation test was used to assess correlation between the variables. Normality was assessed using Shapiro-Wilk test. To compare TBUT and Schirmer test scores of the three groups, Mann-Whitney U test was used. A p-value of ≤0.05 was considered significant.

**RESULTS**

Ninety-seven (n=97) patients were included in the study. Out of the 97 patients, there were forty-five (46.4%) females and fifty-two (53.6%) males, with mean age of 31.31 ± 8.62
Diagnosis of dry eye syndrome using ocular surface disease index, tear film break-up time and Schirmer test

Due to increasing awareness of dry eyes and its impact on visual acuity in a rapidly expanding digital society, self-assessment tool on DES has become crucial for increasing one’s work productivity. OSDI is the common screening questionnaire used by healthcare practitioners to diagnose ocular surface disease. This non-invasive tool can also help individuals in early diagnosis and management without affecting one’s daily activity. Literature had also reported diverse diagnostic criteria of dry eye disease.

An inverse correlation was found between the OSDI and Schirmer, and OSDI and TIBUT test scores which was also statistically significant. Schirmer and TIBUT test scores also showed significant correlation (Table I).

The baseline demographic data, OSDI points, mean test scores for TIBUT and Schirmer tests are summarised in Table II.

No statistically significant difference (Mann-Whitney U test) was seen among TIBUT and Schirmer test scores in patients with normal/mild, moderate and severe disease. The p-value of inter-group comparison is summarised in Table III.

Table I: Correlation analysis among OSDI, TIBUT, and Schirmer test scores.

<table>
<thead>
<tr>
<th></th>
<th>OSDI and TIBUT</th>
<th>OSDI and Schirmer</th>
<th>TIBUT and Schirmer</th>
</tr>
</thead>
<tbody>
<tr>
<td>r-value</td>
<td>-0.314</td>
<td>-0.250</td>
<td>0.513</td>
</tr>
<tr>
<td>p-value</td>
<td>0.002</td>
<td>0.014</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

OSDI: Ocular Surface Disease Index, TIBUT: Tear film break-up time.

Table II: Baseline demographic data, mean OSDI points, mean TIBUT and Schirmer test scores of the study participants.

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n=71)</th>
<th>Group 2 (n=15)</th>
<th>Group 3 (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OSDI point</td>
<td>9.11 ± 7.42</td>
<td>26.25 ± 2.81</td>
<td>44.22 ± 10.38</td>
</tr>
<tr>
<td>TIBUT (s)</td>
<td>10.11 ± 4.68</td>
<td>8.37 ± 4.21</td>
<td>8.22 ± 3.64</td>
</tr>
<tr>
<td>Schirmer test (mm)</td>
<td>25.55 ± 10.67</td>
<td>20.77 ± 10.64</td>
<td>23.66 ± 12.09</td>
</tr>
<tr>
<td>Age (years)</td>
<td>31.61 ± 8.49</td>
<td>34.07 ± 8.28</td>
<td>25.64 ± 8.15</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>41 (57.7%)</td>
<td>8 (53.3%)</td>
<td>3 (27.2%)</td>
</tr>
<tr>
<td>Female</td>
<td>30 (42.2%)</td>
<td>7 (46.6%)</td>
<td>8 (72.7%)</td>
</tr>
</tbody>
</table>

OSDI: Ocular Surface Disease Index, TIBUT: Tear film break-up time, s: Second, mm: Millimetre, Group 1: Normal/mild disease, Group 2: Moderate disease, Group 3: Severe disease, n: Number.

Table III: Intergroup comparison between TIBUT and Schirmer tests (Mann-Whitney U test, p-values).

<table>
<thead>
<tr>
<th></th>
<th>TIBUT</th>
<th>Schirmer</th>
</tr>
</thead>
<tbody>
<tr>
<td>p-value</td>
<td>0.133</td>
<td>0.133</td>
</tr>
<tr>
<td>Group 1–2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 1–3</td>
<td>0.250</td>
<td>0.588</td>
</tr>
<tr>
<td>Group 2–3</td>
<td>0.635</td>
<td>&gt;0.99</td>
</tr>
</tbody>
</table>

Group 1 = Normal/mild disease, Group 2 = Moderate disease, Group 3 = Severe disease, TIBUT = Tear film break-up time.

**DISCUSSION**

Due to increasing awareness of dry eyes and its impact on visual acuity in a rapidly expanding digital society, self-assessment tool on DES has become crucial for increasing one’s work productivity. OSDI is the common screening questionnaire used by healthcare practitioners to diagnose ocular surface disease. This non-invasive tool can also help individuals in early diagnosis and management without affecting one’s daily activity. Literature had also reported diverse diagnostic criteria of dry eye disease.

Hirosawa et al. studied the capacity of Maximum Blink Interval and Japanese-OSDI on assessing dry eye disease (DED) and concluded that both are novel, non-invasive screening test for DES. This current study also showed that OSDI questionnaire is feasible, easily performable tool for self-assessment, with the highest level of validation.

A study by Suman et al. enrolled 100 patients with dry eye symptoms and found statistically significant inverse correlation between the OSDI and TIBUT (r = -0.597) and statistically significant correlation between TIBUT and Schirmer test (r = -0.227), which were similar to the data of this current study, whereas no significant correlation was noted between OSDI and Schirmer’s test (r = -0.142). However, this current study showed statistically significant inverse correlation between OSDI and Schirmer test (r = -0.250).

Unlu et al. also reported a significant inverse correlation between the OSDI and TIBUT scores (r = -0.385), while no significant correlation was noted between OSDI and Schirmer’s test scores. Alves et al. reported variable diagnostic test results among different conditions. However, the best correlation was seen between vital staining and TIBUT, and the best test group to detect DED was OSDI/TIBUT/Schirmer. Ozcura et al. also studied the reliability and diagnostic capability of OSDI for DES and reported an inverse correlation between the OSDI and TIBUT test scores but found no correlation between the OSDI and Schirmer test scores.

Another study by Kalezic et al. showed that the Schirmer 1 test of both eyes (right eye p < 0.001, left eye, p = 0.004) while the Rose Bengal test (p = 0.016) and TIBUT test (p = 0.022) for the left eyes were positively correlated with OSDI score. The current study, however, showed statistically significant inverse correlation between OSDI with Schirmer and TIBUT tests.

Onwubiko et al. also assessed the concordance between the diagnostic tests for dry eye disease (DED) and reported that OSDI is inversely correlated with Schirmer test (p<0.001) and TIBUT (p<0.001). His results are consistent with the current study results.

Since, there is currently no questionnaire that can serve as the gold standard for diagnosing dry eye illness, more research on the subject is required. This study, however, used the standardised, affordable, and easily performable OSDI questionnaire for detection of dry eye syndrome and correlated it with tear break-up time and Schirmer test. Further tests should be carried out for better apprehension of DES mechanism.

There were certain limitations in this study. One of the main pathological mechanisms in dry eye illness had been identified as hyperosmolarity of the tear film. However, tear osmolarity and Rose Bengal staining scores for diagnosis of dry eye were not included in this study. Furthermore, temperature and humidity play a role in dry eyes which were not recorded during this study. Data would have been more representative with a larger sample size in a multicentric study.
CONCLUSION

The OSDI questionnaire was quick, precise, feasible, self-assessment and non-invasive standardised tool for evaluating symptoms of dry eye disease, hence it can aid in the diagnosis of DES.

ETHICAL APPROVAL:
This study was carried out after obtaining an approval from the Institutional Review Board and Ethical Committee of the Armed Forces Institute of Ophthalmology.

PATIENTS’ CONSENT:
Informed consent were taken from all patients who participated in the study.

COMPETING INTEREST:
The authors declared no competing interest.

AUTHORS’ CONTRIBUTION:
SH: Conception and design of the work.
MN: Drafting and data acquisition.
MS: Drafting the work.
SAHN: Data interpretation.
MI: Final approval of the manuscript.
QH: Data analysis.
All authors approved the final version of the manuscript to be published.

REFERENCES


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