



## Original Research Article

## Prevalence of dry eyes in patients with Type-2 diabetes mellitus

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## ARTICLE INFO

## Article history:

Received 14-01-2020

Accepted 05-02-2020

Available online 16-06-2020

## Keywords:

Dry eye

Diabetes

Fluorescein

OSDI

Schirmers test

TBUT

Tear film

## ABSTRACT

**Purpose:** To estimate the prevalence of dry eyes in patients with Type-2 diabetes mellitus and to compare various tests of dry eye.**Materials and Methods:** An analytical cross sectional study was conducted on 150 patients diagnosed with Type 2 diabetes mellitus. Dry eyes symptoms were assessed using Ocular surface disease index (OSDI) questionnaire and graded according to severity. The diagnosis was confirmed by positive Ocular surface staining pattern with fluorescein, Tear film breakup time test (TBUT) or Schirmers test. Severity of dry eyes was determined and prevalence calculated.**Results:** The prevalence rate of dry eye disease among diabetics was calculated as 36% on the basis of Ocular surface disease index. Mild, moderate and severe dry eyes were present in 16%, 16% and 4% patients respectively. TBUT showed very good agreement with highest diagnostic accuracy. Schirmers test and Fluorescein test had good and moderate agreement respectively.**Conclusion:** Diabetes mellitus associated dry eye disease (DMDES) is the most frequent diabetic complication in clinical practice. Clinical trials are warranted to confirm the effects of the currently applied drugs in diabetes-associated DES for a better outcome in such patients. Our study can act as a stepping stone for larger multi-centric studies to gain more information about this largely unrecognized problem of diabetes associated dry eye disease.© 2020 Published by Innovative Publication. This is an open access article under the CC BY-NC license (<https://creativecommons.org/licenses/by-nc/4.0/>)

## 1. Introduction

In 2007, Tear Film and Ocular Surface Society (TFOS) Dry Eye Workshop II (DEWS II) Definition and Classification subcommittee report defined Dry eye disease (DED) as a “multifactorial disease of the ocular surface characterized by the loss of hemostasis of the tear film and accompanied by ocular symptoms in which tear film instability and hyperosmolarity, ocular surface inflammation and damage and neurosensory abnormalities play etiological roles.”<sup>1</sup>

Ocular surface unit consists of cornea, conjunctiva, glands like lacrimal and meibomian glands and lids. All these structures are connected by sensory and motor nerves. Any dysfunction or disturbance in this ocular surface

function unit can lead to dry eyes. This causes grittiness and irritation leading to ocular surface inflammation, signs of ocular surface damage and visual impairment.<sup>2</sup> Severe dry eye results in impairment in daily living, work productivity and affect mood and confidence.<sup>3</sup>

Diabetes causes corneal and conjunctival epithelial damage, inducing reduction of the number of goblet cells and mucin production and the hydrophilic nature of the ocular surface leading to tear film instability. Dry eyes in turn are an important contributor to problems associated with diabetes like superficial punctate keratopathy, trophic ulceration and persistent epithelial defects. The precise role of these abnormalities in the pathogenesis of dry eyes is not well defined. Hence, the relationship between dry eyes and diabetes is not very clear.

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## 2. Materials and Methods

An Analytical Cross sectional study was conducted in the outpatient department of Ophthalmology in a Tertiary Care Hospital of Western Maharashtra from September 2017 to August 2019 on 150 diabetic patients. Patients of age 40-70 years of both sexes diagnosed to have diabetes mellitus were included in the study. Patients who were excluded were cigarette smokers, contact lens users, glaucoma patients, patients with preexisting ocular allergies, ocular surface disorders, lid and adnexal diseases and keratorefractive procedures. Other patients who were excluded were patients with Sjogren's syndrome, Rheumatoid arthritis, Lupus erythematosus, Parkinsonism, Steven-Johnson syndrome, ocular pemphigoid, pemphigus, corneal edema, viral keratitis, Hansens disease, chemical burns, radiation and Vitamin A deficiency. Patients on chronic ocular medications, nutritional tear supplements, local/systemic medications known to cause dry eye such as antihistaminics, tricyclic antidepressants, oral contraceptive pills, beta-blockers and diuretics were also excluded from the study.

Ethical committee clearance and written and informed consent was taken from all patients. Detailed history was taken followed by thorough ophthalmic examination of both the eyes. Visual acuity was assessed-distant vision by Snellen's chart and near vision by Jaeger's chart. Auto Refractometry (Grand Seiko), BCVA (Best Corrected Visual Acuity) and intraocular pressure (measured by Goldmann's Applanation tonometry) was recorded. A detailed slit lamp biomicroscopic examination of anterior segment and dilated retinal status evaluation by 90 D lens was done.

Dry eyes were suspected on the basis of a history of soreness, gritty sensation, itching, redness and blurred vision that improves with blinking and excessive tearing. The symptoms were assessed using Ocular surface disease index (OSDI) questionnaire. It is a self administered 12 item questionnaire of grading of ocular symptoms over a 2 to 4 week period prior to the visit. Values to determine dry eye severity were calculated using the OSDI formula (Sum of score divided by total number of questions answered and multiplied by 25). Score ranges from 0 to 100. After calculating the score, patients were graded according to severity as normal (0-12 points), mild dry eye (13-22 points), moderate dry eye (23-32 points) and severe dry eye (33-100 points)

The diagnosis was confirmed when one or more of the following tests were positive: Ocular surface staining pattern with fluorescein, Tear film breakup time test (TBUT), Schirmers test. Ocular surface staining pattern with fluorescein was observed 1-2 minutes after insertion of commercially available presterilized strip of 2% fluorescein into the lower fornix of each eye. Fluorescein staining under cobalt blue light was graded as 0 (No staining), 1 (Mild

staining occupying < 1/3 of corneal epithelial surface):2 (Moderate staining occupying < 1/2 of corneal epithelial surface, 3 (Severe staining of > 1/2 of the corneal epithelial surface)

Tear film breakup time test (TBUT) was calculated using wet fluorescein-impregnated strip placed in lower fornix and then removed. The time between the last blink and the appearance of the first random dry spot in the pre-corneal fluorescent tear film using broad beam of slit lamp and cobalt blue filter was measured. Normal range is between 15-35 seconds. Appearance of dry spot or line before 10 seconds was considered abnormal and documented as dry eye. Schirmer test I was used using Schirmer strip (commercially available pre-sterilized Whatman Filter paper no.41, 5 mm wide & 35 mm long) which was first folded at the 5 mm marking and was placed at the junction of middle and the outer third of the lower eyelid in the inferior cul-de-sac. After 5 minutes of eyelid closure, both the strips were removed from the fornices simultaneously and wetting of the filter paper strip was measured. Wetting of less than 10 mm was considered abnormal and documented as dry eye.

Dry eye was graded into three types-mild, moderate, and severe.

**Table 1:** Grading of severity of dry eye

Severity of dry eye	Corneal staining with fluorescein	TBUT (in seconds)	Schirmers test score (in mm)
Mild	< 1 Quadrant of punctate staining	<10	<10
Moderate	>1 Quadrant of punctate staining	5-10	5-10
Severe	Diffuse punctate or confluent staining	<5	<5

Using tests of statistical analysis, prevalence of dry eyes was calculated and blood sugar levels- Fasting (BSL-F) and Post prandial (BSL-PP), urine Routine/Microscopy, glycosylated hemoglobin levels were sent.

## 3. Results and Observation

This study is an Analytical Cross sectional study conducted in the Department of Ophthalmology in a tertiary care hospital from September 2017 to August 2019. A total of 150 patients of diabetes mellitus were included in the study. The prevalence of dry eyes was determined using various dry eye tests.

On ocular surface staining of the study eyes with fluorescein, mean grade was  $0.32 \pm 0.73$ . In majority of the eyes studied (81.33%), grade 0 was present; in 8.67% study

**Table 2:** Ocular surface staining of study eyes with fluorescein.

Ocular surface staining of study eyes with fluorescein	Frequency	Percentage
<b>Scoring</b>		
0	244	81.33%
1	23	7.67%
2	26	8.67%
3	7	2.33%
Mean ± Stdev	0.32 ± 0.73	
Median (IQR)	0 (0 - 0)	
<b>Dry eye</b>		
No	244	81.33%
Yes	56	18.67%

eyes, grade 2; in 7.67% study eyes, grade 1; and in 2.33% study eyes, grade 3 was present. 18.67% of eyes studied had dry eye status.

**Table 3:** Dry eye (tear film breakup time test (tbut)) in study eyes.

Dry eye [Tear film breakup time test (TBUT)] in study eyes	Frequency	Percentage
No	207	69.00%
Yes	93	31.00%
Mean ± Stdev	17.04 ± 9.17 seconds	
Median (IQR)	19 (7 - 24) seconds	

When Tear film breakup time test (TBUT) was done, dry eye was present in 31.00% of the eyes studied. Mean value of TBUT was 17.04 ± 9.17 seconds.

**Table 4:** Dry eye (schirmers test) in study eyes

Dry eye (Schirmers test) in study eyes	Frequency	Percentage
No	222	74.00%
Yes	78	26.00%
Mean ± Stdev	16.75 ± 8.47 mm	
Median (IQR)	18 (10 - 22) mm	

In present study, dry eye as diagnosed by Schirmers test was present in 26% eyes studied. Mean value of Schirmers test was 16.75 ± 8.47 mm.

**Table 5:** Severity of dry eye among study eyes based on ocular surface disease index (OSDI).

Severity of dry eye among study eyes based on Ocular surface disease index (OSDI)	Frequency	Percentage
Normal	192	64.00%
Mild dry eye	48	16.00%
Moderate dry eye	48	16.00%
Severe dry eye	12	4.00%
Total	300	100.00%

On the basis of Ocular surface disease index (OSDI), 64% of the eyes studied did not have dry eyes. 16% eyes were categorized into mild dry eyes and moderate dry eye each. 4% eyes studied were severely dry.

Specificity of both Ocular surface staining pattern with fluorescein and TBUT was 100% each for predicting dry eye symptoms and of Schirmers test was 94.79%. Sensitivity of TBUT was maximum (86.11%) as compared to Ocular surface staining pattern with fluorescein (51.85%) and Schirmers test (62.96%).

Area under curve (AUC) of TBUT was excellent (0.93) with 95% CI of 0.90 to 0.96 and AUC of Ocular surface staining pattern with fluorescein and Schirmers test was good; 0.76 (0.71 to 0.81) of Ocular surface staining pattern with fluorescein and 0.79 (0.74 to 0.83) of Schirmer's test. Diagnostic accuracy was also highest in TBUT as compared to other two tests. There is always a trade-off between sensitivity and specificity (any increase in sensitivity will be accompanied by a decrease in specificity) so we choose that variable as best in which combination of sensitivity and specificity gives the maximum predictive value. In our study, therefore, TBUT was the best predictor of dry eye symptoms as compared to Schirmers test and Ocular surface staining pattern with fluorescein.

#### 4. Discussion

There has been a great progress in our understanding of the ocular surface in the last decade. An increasing prevalence of Diabetes-Associated Dry Eye Syndrome (DMDES) has been reported in recent years.<sup>4</sup> The pathogenesis and specific features of DMDES remain uncertain and general interventions are limited to those used in DES; and not targeted against diabetes associated dry eyes.

Thus, an Analytical Cross sectional study was conducted to estimate the prevalence of dry eyes in diabetes. We studied 150 diabetic patients (300 eyes) and found a dry eye prevalence rate of 36%. Literature reports show varied prevalence of dry eyes. In a latest study conducted in China, Zou X et al. (2018)<sup>5</sup> reported dry eyes prevalence rate as low as 17.5% and on the other hand, Manaviat MR et al.<sup>6</sup> reported a prevalence rate as high as 54%. Among Indian studies, Choudhary P et al.<sup>7</sup> found prevalence of dry eye in eastern Madhya Pradesh as 9.6%. Sahai and Mallik<sup>8</sup> reported a prevalence rate of 18.4% in West Bengal. Titiyal JS et al. (2018)<sup>9</sup> reported a prevalence rate of 32% in North India.

Various reasons can be attributed to the large variation in the prevalence rates of dry eyes in diabetics (DED). Firstly, different diagnostic criteria might affect the prevalence of dry eyes reported in the present and previous studies. Manaviat MR et al.<sup>6</sup> performed Schirmers and Tear film breakup time test (TBUT) tests and utilized the criterion of one positive test to establish the diagnosis in type 2 diabetic patients. Another such study used tear osmolarity values to

**Table 6:** Diagnostic test for predicting dry eye symptoms in study eyes.

Dry eye symptoms in study eyes	Sensitivity (95% CI)	Specificity (95% CI)	Area Under Curve (AUC)	Positive Predictive Value (95% CI)	Negative Predictive Value (95% CI)	Diagnostic accuracy
Dry eye (Ocular surface staining pattern with fluorescein)	51.85% (42.03% to 61.57%)	100% (98.10% to 100.00%)	0.76 (0.71 to 0.81)	100% (93.62% to 100.00%)	78.69% (73.01% to 83.65%)	82.67%
Dry eye (Tear film breakup time test (TBUT))	86.11% (78.13% to 92.01%)	100% (98.10% to 100.0%)	0.93 (0.90 to 0.96)	100% (96.11% to 100.00%)	92.75% (88.33% to 95.89%)	95.00%
Dry eye (Schirmers test)	62.96% (53.14% to 72.06%)	94.79% (90.63% to 97.47%)	0.79 (0.74 to 0.83)	87.18% (77.68% to 93.68%)	81.98% (76.28% to 86.80%)	83.33%

diagnose DED in their study.<sup>10</sup> In a study conducted in 2018 by Titiyal JS et al.,<sup>9</sup> Ocular Surface Disease Index (OSDI) scores were used to assess dry eyes. Similarly, in our study, different objective tests have shown different prevalence rates of dry eyes.

Among the subjective tests, dry eye symptoms are scored by questionnaires. Two validated, reliable and currently available dry eye questionnaires that are in accordance with the FDA-PRO (Food and Drug Administration-Patient Reported Outcome) guidelines are OSDI and the Impact of dry eye on everyday life (IDEEL) questionnaire. In our study, we used the OSDI questionnaire as the basic tool for screening the patients for dry eye. Shorter completion time, easy comprehension by patients and no additional cost make OSDI ideal for clinical use in the outpatient department.<sup>9</sup> In our study, OSDI showed a 36% prevalence of dry eyes and the comparison of other tests with OSDI has been shown in the Table 7.

**Table 7:** Objective diagnostic tests used in our study

Tests	Dry eyes (%)	Diagnostic accuracy	Kappa agreement*
Fluorescein test	18.67%	82.67%	0.580
TBUT	31%	95.00%	0.888
Schirmers test	26%	83.33%	0.615

\*In comparison to OSDI

Though several objective tests have been developed to diagnose and grade the severity of DED, these tests show poor repeatability, significant interobserver variability and correlate poorly with the symptoms and quality of life of the patient. In our study, TBUT showed very good agreement with OSDI (Subjective scoring) with the highest diagnostic accuracy among the objective tests; Schirmer’s test and Fluorescein test showed good and moderate agreement respectively. All the objective tests reported less prevalence of dry eyes as compared to that reported by OSDI subjective scoring. Thus, OSDI dry eye prevalence was taken as final for assessment in our study.

There has been a growing prevalence of DM in India (65.1 million, 2016) in the recent years. While diabetic retinopathy (DR) and diabetic cataracts are well-known complications, dry eye syndrome (DES), is increasingly becoming common in the diabetic population.

Thus, we conclude that in addition to the DR which is the leading cause of blindness, more attention should be paid to diabetes mellitus associated dry eye disease (DMDES) which is the most frequent diabetic complication in clinical practice. Additional clinical trials are warranted to confirm the effects of the currently applied drugs in diabetes-associated DES for a better outcome in such patients.

## 5. Conclusion

The prevalence rate of dry eye disease among diabetics was calculated as 36% on the basis of Ocular surface disease index. Mild, moderate and severe dry eyes were present in 16%, 16% and 4% patients respectively. TBUT showed very good agreement with highest diagnostic accuracy. Schirmers test and Fluorescein test had good and moderate agreement respectively.

Our study was a single center study conducted on 150 patients without controls and long term follow up. Thus, it can act as a stepping stone for larger multi-centric studies to gain more information about this largely unrecognized problem of diabetes associated dry eye disease.

## 6. Source of Funding

None.

## 7. Conflict of Interest

None.

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**Cite this article:** Aggarwal M, Goud R, Radhakrishnan OK, Mantri P, Shah A. Prevalence of dry eyes in patients with Type-2 diabetes mellitus. *Indian J Clin Exp Ophthalmol* 2020;6(2):286-290.