



## Dry Eye Occurrence in Type II Diabetics and Non-diabetics: A Prospective Cohort Study

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### Abstract

**Purpose:** To compare the prevalence and severity of dry eye in Type 2 diabetics with non-diabetics.

**Methods:** A total of 200 eyes of 200 patients; 100 patients whom were diagnosed cases of type 2 diabetes and 100 non-diabetics who presented with ocular discomfort were evaluated over 12 months. Right eye was taken up for the study in all the patients. Dry eye was confirmed by diagnostic tests namely: Schirmer's test, Tear break up time, Tear meniscus height, Fluorescein staining and Lissamine green staining. Ocular Surface Disease Index questionnaire was filled. On the basis of symptoms, signs and test results, Dry eye was graded from grade 1 to grade 4 according to the Dry eye workshop dry eye severity grading scheme.

**Results:** Most patients (82%) above the age of 50 were diabetics. Diabetics presented to the clinic nearly eight years later than non-diabetics ( $p < 0.0001$ ). Itching (In Non-diabetics) and grittiness (In diabetics) were the most common symptoms ( $p = 0.04$ ). Schirmer's test and Tear Break up time was found to be abnormal in more diabetics as compared to non-diabetics. Tear meniscus height was similar in both groups. Diabetics also had much higher grade of dry eye disease ( $p$  value = 0.002). Prevalence of dry eye among diabetics was 43 % while in non-diabetics was 30 %.

**Conclusion:** Patients in diabetic group had higher grade of dry eye as compared to non-diabetic patients. Schirmer's test value was significantly lower in diabetics than non-diabetics.

**Keywords:** Diabetes Mellitus (DM); Tears; Xerophthalmia

### Introduction

Diabetes is quickly emerging as one of the biggest health related catastrophe the world has ever witnessed [1]. The World Health Organization estimates that there will be 370 million people with diabetes on the planet by 2030 [2].

Diabetes is often associated with several significant ocular conditions, such as retinopathy, refractive changes, cataract, nerve

palsies, glaucoma and macular edema. However, recently problems involving ocular surface, dryness in particular has been reported and has become the biggest issue with advent of computers [3].

Corneal complications of dry eye syndrome include superficial punctate keratopathy, corneal ulcerations, persistent epithelial defects, filamentary keratitis and these can be sight threatening but the most common dry eye symptoms reported by patients are burning and foreign body sensation [4,5].

The diagnosis of dry eye syndrome is made from a combination of the clinical history, suggestive constellation of abnormalities on Schirmer's and Tear breakup time (T-BUT testing), fluorescein staining, and rose bengal staining and if available, confirmatory laboratory evidence of increased tear osmolarity and decreased reflex lactoferrin levels [6].

The early diagnosis of dry eye syndrome in diabetic patients is important to prevent complications. Studies to evaluate the prevalence of dry eye syndrome in type 2 diabetic patients are lacking and there is scarcity of studies relating to prevalence of dry eyes and ocular surface disorders in diabetic patients in Indian context. Hence the present study was undertaken to compare occurrence of dry eye among type II diabetic patients and non-diabetics.

## Materials and Methods

This prospective cohort study was done over 12 months at a tertiary hospital in Southern India and approval for the study was taken from Institutional Ethical Committee and declaration of Helsinki (1975) and as modified in 2000 and 2008 were adhered to. Informed consent was taken from all patients.

Patients coming to the ophthalmology outpatient department for disturbance of ocular surface and fulfilling the inclusion and exclusion criteria were taken for the study. A total of 200 consecutive patients who presented with history of ocular discomfort were included under the study of which 100 were normal subjects and 100 cases of Diabetes Mellitus (DM) were examined. Patients with at least five years of history of being diagnosed with type 2 DM were taken for the study. Equal distribution was done amongst the groups for better statistical analysis.

Patients with ocular surface disease symptoms such as grittiness, itching, burning sensation, early morning stickiness, redness, watering, photophobia were included in the study and were divided into two groups based on their diabetic status.

Cigarette smokers, contact lens users, patients with history of refractive surgery, patients suffering from diseases such as atopy, Sjogren's syndrome, Rheumatoid arthritis, Parkinson's disease, lupus, and patient on medications such as antihistamines, tricyclic antidepressants, oral contraceptives, and anti-hypertensives and diuretics were excluded from the study.

## Procedure

After enrollment, patients were interviewed for the demographic data and detailed history followed by general and systemic examination.

Dry eye disorder was suspected on the basis of a history of ocular symptoms including soreness, gritty sensation, itchiness and redness, blurred vision that improved with blinking, and early morning stickiness. Ocular examination included recording visual acuity with Snellen's chart, slit-lamp biomicroscopic examination for condition of lid, meibomian gland and conjunctival surface. Cornea was evaluated for its sheen, surface (superficial punctate keratitis/filamentary keratitis/mucous plaques) and sensations. Detailed fundus examination with direct and indirect ophthalmoscope for grading of diabetic retinopathy, if present was done.

Dry eye was confirmed by ocular surface dye staining pattern with fluorescein and lissamine green stain; Ocular Surface Disease Index questionnaire which was filled by the patients and three diagnostic tests namely, Schirmer's Test (less than 10mm in 5 min taken as positive), Tear film break up time (less than 10mm taken as positive), Tear meniscus height mean (TMH) values of less than 0.25 mm taken as positive were performed [7].

Diagnosis was established by positivity of one or more of the tests (T-BUT or Schirmer test) and grading was done according to the Dry eye workshop dry eye severity level grading system [8].

## Statistical analysis

Random sampling technique was used to categorize the patients amongst the two groups. Chi square test was done to calculate the p values. Tables were made using Microsoft Excel 2017, and Microsoft word 2017 was used to make the article file. SPSS software version 26 was used to do statistical analysis. P value less than 0.05 was considered significant,

## Results

The present study was conducted on 200 eyes of 200 patients, 100 patients diagnosed cases of type II DM and 100 non-diabetics. Schirmer's test, T-BUT time, TMH and grading of dry eye were analyzed in all patients.

Mean duration of diabetes among diabetic patients was  $7.1 \pm 5.9$  years. It was observed that diabetic patients developed dry eyes at a later part in life as compared to non-diabetics with over 82% patients above the age of 50 being diabetics (Table 1). Statistically it was seen that diabetics presented to the clinic nearly eight years later than non-diabetics ( $p < 0.0001$ ).

Diabetics were found to have significantly more patients with Schirmer's less than 10mm (Table 2) at the end of five min ( $p < 0.001$ ). More patients were found to have normal T-BUT values (Table 3) in the diabetic group though it was found to be statistically insignificant ( $p = 0.8$ ). TMH also was found to have a near equal distribution amongst the diabetics and non-diabetics.

Age (years)	Non-diabetics		Diabetics	
	n	%	n	%
<40	24	24.0	0	.0
41-50	26	26.0	18	18.0
	34	34.0	48	48.0
51-60	16	16.0	34	34.0
>61				

**Table 1:** Age distribution of study participants.

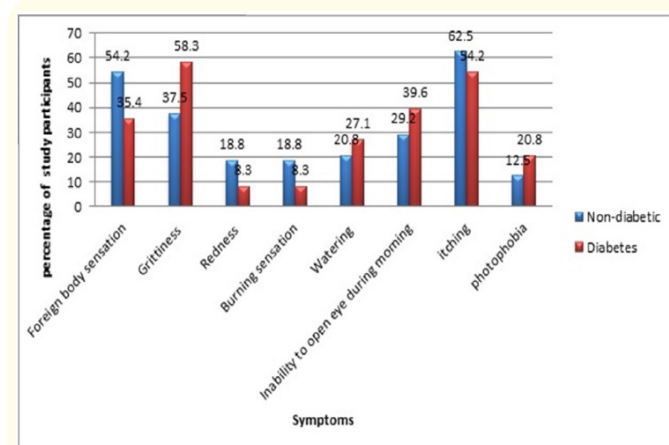
Amongst the symptoms it was observed that itching and grittiness were the most common symptoms with which the patients presented to the dry eye clinic. Amongst diabetics, grittiness was the predominant symptom being seen in 58.3% patients. It was the most significant symptom also with a p value of 0.04. Itching (62.5%) and foreign body sensation (54.2%) were the most common symptoms in patients with no history of diabetes (Figure 1).

Schirmer's test value	Non-Diabetics		Diabetics	
	N	%	N	%
1 - 5	4	4.0%	14	14.0%
5 - 10	8	8.0%	19	19.0%
	88	88.0%	67	67.0%
>10				

**Table 2:** Schirmer's Test Value between the two groups.

T-BUT value	Non-Diabetics		Diabetics	
	N	%	N	%
1-5	8	8.0%	18	18.0%
5-10	22	22.0%	25	25.0%
	70	70.0%	57	57.0%
>10				

**Table 3:** TBUT values between the two groups.



**Figure 1:** Symptoms of patients in the two groups.

Overall comparing the dry eye severity amongst the diabetics and non-diabetics it was found that diabetics had much higher grade of dry eye disease ( $p$  value = 0.002) with nearly 37% patients had severe dry eye disease in the diabetics group as compared to 15% of the non-diabetics group (Table 4).

Grade of dry eye	Non-Diabetics		Diabetics	
	N	%	N	%
0	70	70.0%	57	57.0%
	15	15.0%	6	6.0%
1	11	11.0%	26	26.0%
	4	4.0%	11	11.0%
2				
3				

**Table 4:** Grading of dry eye between the two groups.

Prevalence of dry eye in diabetics was 43 % and 30 % in non-diabetics.

## Discussion and Conclusion

Diabetes has rapidly become one of the leading systemic risk factors for dry eye. This present study was an attempt to find out the prevalence and disease pattern of dry eyes in patients of type 2 diabetes in comparison with non-diabetics.

The prevalence of dry eye in the present study for diabetic group was 43% and for non-diabetic group was 30 %, this was similar to older studies where prevalence of dry eye disease was found to vary between 18.4% and 40.8% [9-12].

Diabetics were also found to be about eight years older than non-diabetics in this study. Unlike our study, several previous studies have not found any correlation between age and dry eye syndrome [13,14]. Though as diabetes is expected to develop in later part of life and its complications even more later, it is possible that there may be a selection bias when correlating age and dry eye disease in diabetics.

It was also observed that diabetics had a higher grade of dry eye disease as compared to non-diabetics.

Schirmer's value was significantly lower in diabetic group as compared to non-diabetics. Cohen's kappa coefficient was used to assess reliability amongst the three objective tests. Schirmer's test and T-BUT showed good level of agreement with kappa value of 0.67 while Schirmer's test and TMH as well as T-BUT and TMH had fair level of agreement with kappa value 0.47 and 0.49 respectively suggesting that these three diagnostic tests were well correlated to each other for diagnosis of dry eye. No patient in our study was found to have grade 4 of dry eye severity. This may have been because such patients would have presented as emergency rather than as outpatient and would not have been included in the study.

Our study results differed from that by a recent study of Beckman who found no difference in the dry eye severity in between diabetics and non-diabetic patients [15]. This may have been due to the fact that they had not excluded patients with recent onset of diabetes and diabetic complications such as diabetic neuropathy which may be a cause of dry eye might not have set in.

Our results were very similar to German scientists Seifart and Stempel who not only found a substantial difference of severity of dry eye amongst the two groups but also established that severity of dry eye disease was directly related with Glycosylated hemoglobin (HbA1C) values. We did not compare the severity of dry eye disease with HbA1C in our study but it can be presumed that the values were near normal as they all were under intense and regular treatment by an endocrinologist [16].

Our results are also in line with a recent meta-analysis conducted by Yoo et al that followed up case control studies of over 18 years and established that diabetes mellitus has a significant association with risk of dry eye [17].

It is still not clear why diabetic patients develop dry eyes more often than non-diabetic subjects. Fox et al has proposed that a possible explanation could be an exocrine dysfunction of the main lacrimal gland in patients with DM.<sup>18</sup> Development of additional unknown proteins in the tear fluids or a microvascular damage of lacrimal gland along with autonomic neuropathy leading to impaired function of the lacrimal gland are some other postulated hypothesis [3].

The decrease in sensitivity of the cornea in patients with diabetic retinopathy is a well-known fact that has been reported in studies such as by Downie and Newell [19]. The diminished sensitivity may be a kind of diabetic neuropathy and thus lead to the reduction of stimulatory signals from the ocular surface to the lacrimal gland and thus influence on regulatory systems.

Another possible reason can be the fact that people with DM have circulating ascorbic acid concentrations at least 30% lower than people without DM. Human tears are rich in vitamin C which acts protectively for the ocular tissues and this preventive action maybe deficient in patients with DM. Moreover, ocular tissues possibly have highest free radical activity in comparison to any other organ, mainly because of ultraviolet exposure. Higher levels of Nitrous oxide found in the aqueous humor of diabetic patients may induce inflammatory reactions that may cause cell damage [20].

This awareness of association of dry eye with diabetics helps us to have high index of suspicion for diagnosis of dry eye in diabetic

patients. Early diagnosis of dry eye syndrome among diabetic patients is important for initiation of treatment therapy which leads to ease of discomfort and prevents further complications. It also contributes towards preventing a very distressful and prolonged period of epithelial non-healing following trauma, infections and in post-operative period of patients who undergo cataract surgery or refractive surgeries

The study had several limitations. The sample size of the study was fairly small. We also did not assess the severity of diabetes and compare with dry eye disease which would have been an ideal scenario. Also, corneal sensitivity was not assessed using tests such as blink rate and corneal wisp test to look for diabetic neuropathy of the corneal nerves.

Our study observed that diabetics have more common symptoms as compared to patients with no history of diabetes. They also have lower Schirmer's test value which may be due to reduced aqueous layer secretion secondary to impaired lacrimal gland function. No significant difference in T-BUT values or TMH was found in the groups in our study.

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### Disclosures

None.

### Conflicts of Interest

None.

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