## Original Articles

# A Comparative Study of Tear Film Tests in Diabetic and Non-diabetic Patients - A Cross - Sectional Study.

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## ABSTRACT

**Aim :** To compare the results of various tear film tests in control and diabetic patients. **Materials and methods :** This observational study included diabetic patients (n=75) and healthy subjects in control group(n=75). All subjects were asked for a detailed history,underwent proper general and systemic examination. Complete ocular examination included best corrected visual acuity, slit lamp examination, intraocular pressure,dilated fundus examination. Tests for dry eyes likes Shirmer's test, tear film break up time(TBUT) , Tear meniscus height,Rose Bengal staining was done on all patients. **Results :** The values of various tear films tests were reduced in diabetic patients as compared to control patients. Shirmer's test showed significantly different results of 23.49±7.98mm vs 17.19±9.54 mm ,p <0.0001 for right eye and 24.8±7.66 mm vs 18.44±10.5mm ,p=0.0001 for left eye.TBUT also showed a significantly different result in both groups as for right eye 11.9±2.07 seconds vs 9.16±3.37 seconds ,p<0.001 for right eye and 11.97±2.01 seconds vs 9.50±3.10 seconds,p>0.0001 for left eye.Tear meniscus height showed significantly different result for both groups of 0.81±.026 mm vs 0.56±0.32 mm,p<0.0001 for right eye and 0.79±.023 mm vs 0.57±.032 mm, p<0.0001 for left eye. Rose bengal staining didn't show much significant result for right eye but was significant for left eye. It did not give a reliable result. **Conclusion :** Dry eye is a significant ocular disorder in diabetic patients and should be taken into account while examination.The results of tear films tests were significantly reduced in diabetic patients.

## INTRODUCTION

A multifactorial disease of the ocular surface characterized by deficient tear production and/or excessive tear evaporation, leading to loss of homeostasis of the tear film.

Cornea, conjunctiva, lacrimal glands, meibomian glands and lids make up the ocular surface unit. Function of this unit is tear film maintainence. Dry eyes occur when there is a dysfunction of this unit. This leads to instability of tear film and breakup of the film before the next blink. The symptoms are transient mild irritation, persistent dryness,itching, burning, redness,pain,ocular fatigue and visual disturbance. Severe dry eye results in impairment in daily living, work productivity and affect mood.[1]

Diabetes is one of the common causes of blindness in persons aged 20-70 years. Cataract and retinopathy are well known ocular complications of diabetes. However, recently, attention has been drawn to ocular surface problems, especially dry eye in diabetic patients.[2] Diabetic keratoepitheliopathy is sometimes hard to cure and can induce quantitative and qualitative abnormalities in tear secretion, contributing to decreased corneal sensitivity and poor adhesion of regenerating epithelial cells.[2,3] Research shows that most cases of dry eye associated with diabetes are caused by insufficient production of tears due to "autonomic neuropathy" affecting the nerves that control the lacrimal gland.[4]

The prevalence of dry eye in diabetes is studied to be 20-55%.[5,6] With the increasing incidence of diabetes it is important to study its long term effects on eyes. Diabetes is one of the leading causes of blindness in older people. Elderly diabetic patients are at a high risk of developing Dry Eye Syndrome (DES), because of the diabetes-induced decrease in corneal sensation, which leads to a decrease in tear production and, therefore, dry eyes. This mechanism is similar to that observed in subjects using corneal contact lenses. Although epidemiologic evidence obtained on the prevalence of DES among diabetic patients is limited, some studies have shown a correlation between diabetes mellitus and DES.[7,8,9]

Possible reason for this may be the diabetic sensory or autonomic neuropathy or the occurrence of microvascular changes in the lacrimal gland.[10]

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This study will evaluate the dry eye in diabetic patients and compare the results with normal people and help identify the changes in eyes that cause discomfort and in severe cases damage to the eyes.

## MATERIALS AND METHODS

A Comparative, cross-sectional study was carried out on out patient department (OPD) patients in our hospital within a duration of 9 months.

**Inclusion Criteria -**

- All patients giving written and informed consent for the study.
- Normal patients without any systemic disease who come for normal routine eye check up.
- The patients having Type II Diabetes for 5 years or more.
- Patients in the age group of 40-70 years.

**Exclusion Criteria -**

- All patients not giving consent for the study.
- Any congenital lacrimal dysfunction.
- Patients instilling any topical drops.
- Patients who have undergone any ocular surgery .
- Patients with any other ocular disorders like conjuctivitis, keratitis, pterygium etc.
- Patients allergic to fluorescein dye.
- Patients with any systemic disorders like hypertension, thyroid, rheumatoid arthritis etc.

Patient selection -

After taking into consideration the inclusion and exclusion criteria, 150 patients attending eye opd, 75 diabetic and 75 non diabetic were selected.

- Ethical committee clearance :

Ethical committee clearance was taken before starting the study.

- Informed consent :

Written and informed consent was taken from all patients who participated in the study.

150 patients were examined – 75 diabetic and 75 normal non-diabetic.

- Detailed history was taken including chief complaints, past history , family history , personal history, drug history followed by general and systemic examination and monitoring of vitals.
- Patients history about diabetes was asked and related reports analysed.
- Patients was examined under torch light of any abnormalities of eyebrows , eyelids , conjunctiva, cornea , sclera, iris , pupil and lens.

- All patients underwent:

- Visual assesment using Snellen's visual acuity chart,
- Examination of anterior segment in detail using slit lamp biomicroscopy.
- Refraction
- Intraocular pressure measurement using non-contact tonometer.
- Fundus examination with direct ophthalmoscope.

Examination for dry eyes

**Schirmer's Test :**

The patient was explained about the entire procedure. The strip was shown to the patient.The patient was seated comfortably at the slit lamp.The test was performed by using a schirmer's strip (Whatman filter paper no.41 ,5mm wide and 35 mm long).The strip was first folded at 5mm mark and placed in the lower lid at junction of middle and outer third. Care must taken not to touch the cornea.Both the eye were examined simultaneously .After 5minutes both the strips were removed from the fornices and wetting of the filter paper strip was measured from the fold.

Wetting of less than 10mm was considered abnormal.

Value of 5-10mm are suggestive of moderate to mild dry eye and less than 5mm are suggestive of suggestive of severe dry eye.

**Tear Film Break up Time :**

The patient was explained the procedure. After a fluorescein strip moistened with sterile saline has been applied to the tarsal conjunctiva in the lower fornix and the patient asked to blink a few times, the strip is removed. The patient was comfortably seated at slit lamp and the tear film is evaluated using a broad beam of the slit lamp with cobalt blue illumination. The patient asked to blink a few times and then asked not to blink and observed on slit lamp.

The time lapse between the last blink and the appearance of the first randomly distributed dry spot on the cornea is the TBUT. The appearance of dry spots in less than 10 seconds is considered abnormal.

**Tear meniscus height :**

For evaluation of the tear volume,the patient was explained the procedure. The fluorescein strip wetted and placed in lower fornix as done for TBUT. Then patient seated at slit lamp and tear meniscus height measured in horizontal slit.

**Rose Bengal staining :**

The patient is explained about the procedure. It was

performed using a saline moistened strip. The saline drop was used to moisten the strip left to remain in contact with the strip for at least a minute to achieve an adequate concentration of Rose Bengal to stain the ocular surface. Patients should be informed that the drop might irritate the eye. The patient is seated at the slit lamp and observed for staining of the cornea and conjunctiveal areas. Rose bengal stain stains the degenerated and devitalized epithelium of ocular surface. The grading of Rose Bengal staining was done by Oxford classification. (photo I)

Dry Eye Study Workshop (DEWS) severity grading :

The severity of dry eye was decided according to the DEWS severity grading. (photo II)

## OBSERVATION :

In this study continuous data were summarised as Mean ± SD (standard deviation) whereas discrete in number (n) and percentage (%). Continuous two independent groups were compared with Mann Whitney U test whereas categorical (discrete) were compared by chi-square ($\chi2$) test. A two-tailed ($\alpha=2$) $p<0.05$ was considered statistically significant. Analyses were performed on Graphpad Instat software (version 2.1).

A total of 300 eyes of 150 patients were examined . The participants were divided in 2 groups .Group A consisting of 75 patients who were non-diabetic and Group B consisting of 75 diabetic patients.Group A was considered to be control.

The primary outcome was to study the relation between dry eyes and diabetes.The secondary outcomes were to study relation between

- Age and dry eyes,

- Gender and dry eye

- Diabetic retinopathy and dry eye.

- Duration of diabetes and dry eye.

The objective was to compare the outcomes between two groups.

The age of patients  ranged from 41 to 70 years. The mean age in control group was 57.89±7.21 years and mean age in diabetics was 57.49±7.54 years.

Comparing the mean age of two groups, Mann Whitney U test showed similar age between the two groups (57.89±7.21years vs 57.49±7.54 years. , U=2901.5, p=0.739) i.e. did not differ significantly.

There were 42 males and 33 females in the control group and 38 males and 37 females in the diabetic group. (fig I)

Comparing the sex proportion (M/F) of two groups, $\chi2$ test showed similar sex proportion between the two groups

($\chi2=0.428$, $p=0.512$) i.e. also not differ significantly.

The above comparisons concluded that the subjects of two groups were age and sex matched and thus comparable and thus may also not influence the study outcome measures.

In both the groups and almost all age groups males were observed to be more.There were more patients in the age group of 61-70 years. (FIG II AND FIG III)

According to schirmer's test 4 out 75 control group patients showed dry eyes in right eye and 2  in left eye. 25 out 75 diabetic group patients showed dry eyes in right eye and 21  in left eye.In diabetic patients males were observed to have more dry eyes than females . Maximum patients with dry eyes were seen in diabetic group and in the age group of 61-70years age group.(FIG IV)

According to tear filmbreakup time,in control group only 7 patients had dry eyes in right eye and 6 patients had dry eyes in left eye.Whereas in diabetic group a total of 36 patients had dry eye in right eye and 32 patients had dry eyes in left eye.In this test also ,in diabetic group, maximum patients with dry eyes were observed in 61-70 years old age group and minimum in 41-50 year with males more than females.(FIG V)

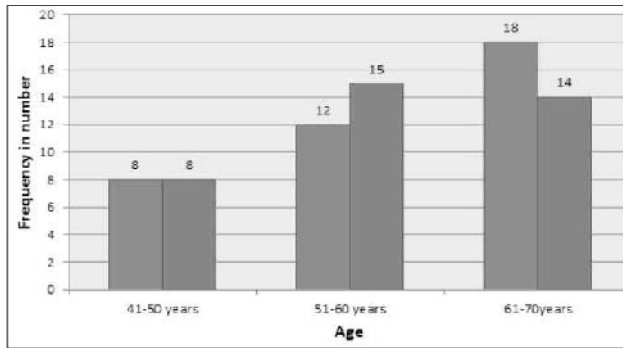According to tear meniscus height, in control group only 6

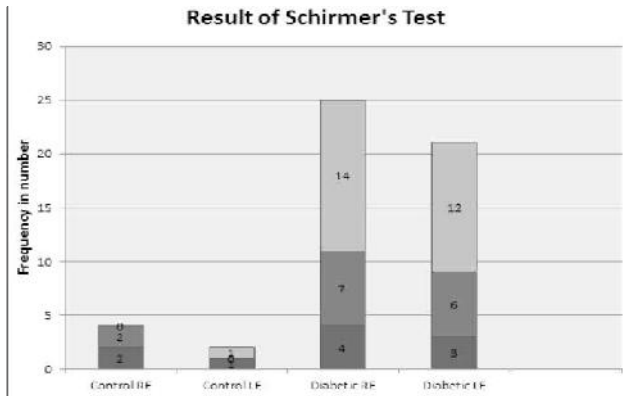**FIG. I. - Distribution of gender  in both groups.**
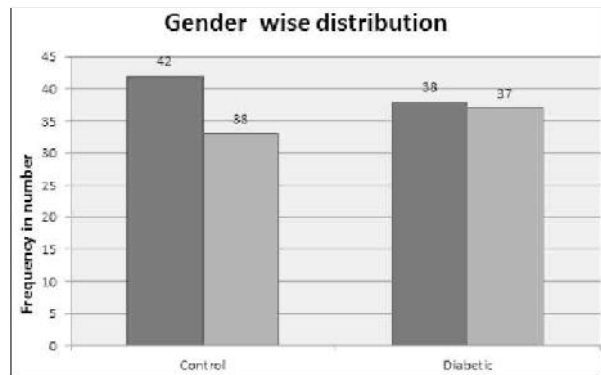


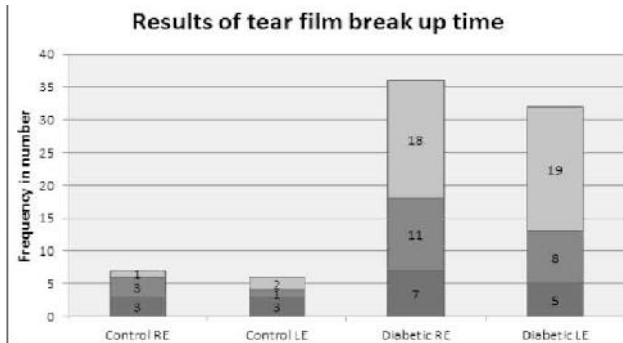**FIG. II. - Age and Gender distribution in control group.**
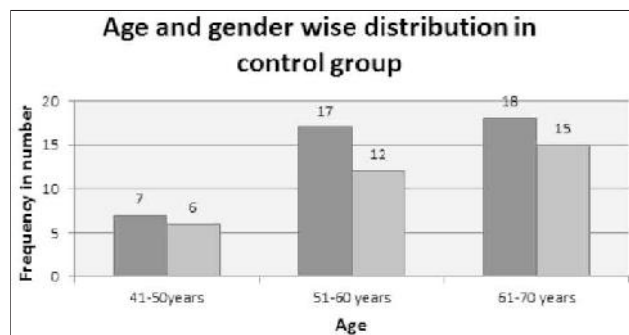
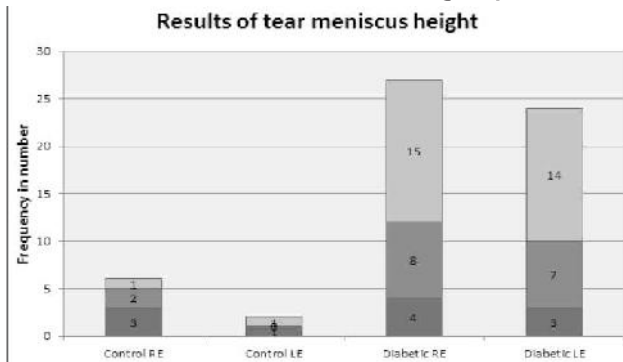**FIG. III. - Age and Gender distribution in diabetic group:**



**FIG. IV. : Comparison of schirmer's test in control and diabetic group:**
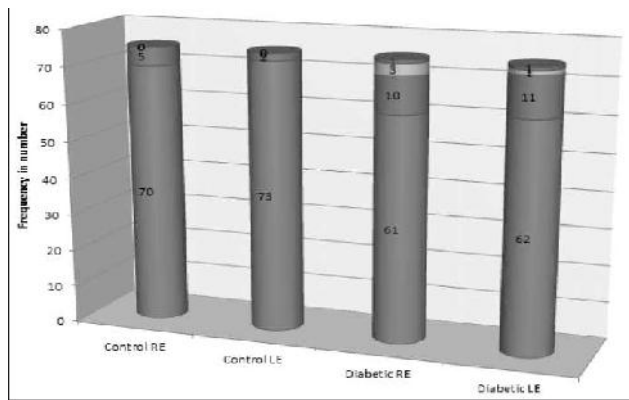


**FIG V: Comparison of tear film break up time data between control and diabetic group:**



**FIG VI : Comparison of tear meniscus height data between control and diabetic groups :**



**FIG VII : Results of Rose Bengal staining :**



**FIG VIII : Graph showing Number of patients with dry eye according to DEWS grading.**
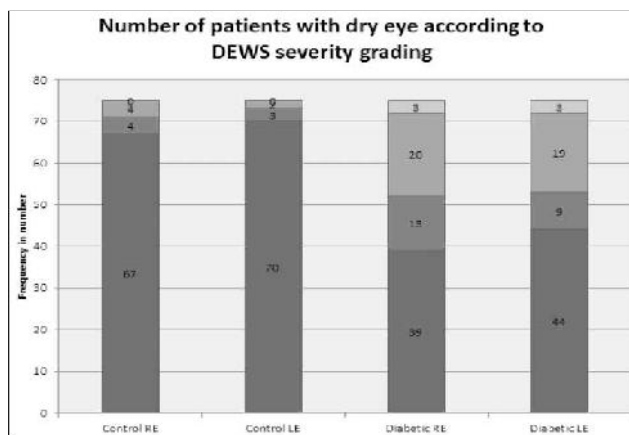


**FIG IX : Chart showing percentage od patients with dry eye in diabetic group graded by DEWS grading.**



Dry eyes

51%

49%

**FIG X : Graph showing percentage of patients having dry eye in diabetic patients with diabetic retinopathy.**



Dry eyes in diabetic retinopathy

33%

67%

**Table I : Mean, Standard deviation and comparison of means.**

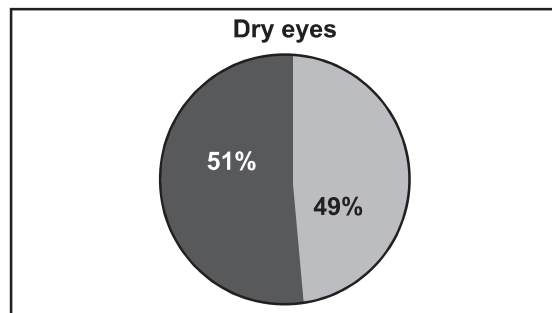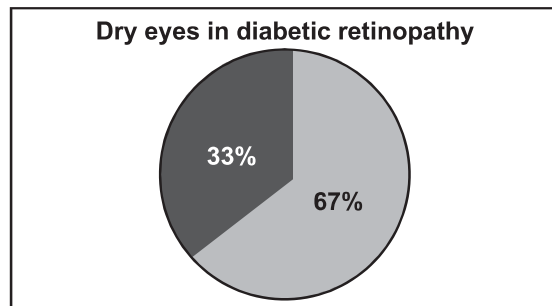| | | CONTROL (Mean ± SD) | DIABETIC (Mean ± SD) | t | p value |
|---|---|---|---|---|---|
| SCHIRMER'S TEST(mm) | RE | 23.49±7.98 | 17.19±9.54 | NA | <0.0001# |
| | LE | 24.8±7.66 | 18.44±10.5 | 4.23 | <0.0001 |
| TBUT (seconds) | RE | 11.9±2.07 | 9.16±3.37 | 6.007 | <0.0001 |
| | LE | 11.97±2.01 | 9.50±3.10 | 5.76 | <0.0001 |
| TEAR MENISCUS HEIGHT (mm) | RE | 0.81±.026 | 0.56±0.32 | NA | <0.0001# |
| | LE | 0.79±.023 | 0.57±0.32 | 4.81 | <0.0001 |

**Table II : Duration of diabetes and patients with dry eyes.**

| Years of diabetes | No. of patients with dry eye | No. of patients in this group | Percentage of patients with dry eye in each group |
|---|---|---|---|
| 5 | 7 | 17 | 41% |
| 6 | 5 | 16 | 31% |
| 7 | 10 | 20 | 50% |
| 8 | 7 | 11 | 63% |
| 9 | 5 | 8 | 62% |
| 10 | 3 | 3 | 100% |
| Total | 37 | 75 | |

patients had dry eye in right eye and 2 patients had dry eyes in left eyes based on tear meniscus height. In diabetic group 27 patients had a low tear meniscus height indicating dry eye in right eye and 24 patients had dry eye in left eye.

Similar to above observation maximum patients were in 61-70 years age group and minimum in 41-50 years and males were more than females.(FIG VI)

The mean value of schirmer's test results (mm) in control group was 23.49±7.98 in right eye and 24.8±7.66 in left eye and mean in diabetic group was 17.19±9.54 and 18.44±10.5 in right and left eye respectively with p value =0.0001.This shows that there was a significant difference in schirmer's test results in between both groups.

While observing tear film break up time (seconds) we observed a mean of 11.9±2.07 in right eye and 11.97±2.01in left eye in control group whereas a mean of 9.16±3.37 in right eye and 9.50±3.10 in left eye with p value <0.0001 which was significant.

In measuring tear meniscus height(mm) a mean of 0.81±.026 and 0.79±.023 was observed in control group for right and left eyes.In diabetic group mean values were 0.56±0.32 and 0.57±0.32 for right and left eyes. The value was <0.0001 which suggested a significant difference in result values.(TABLE I)
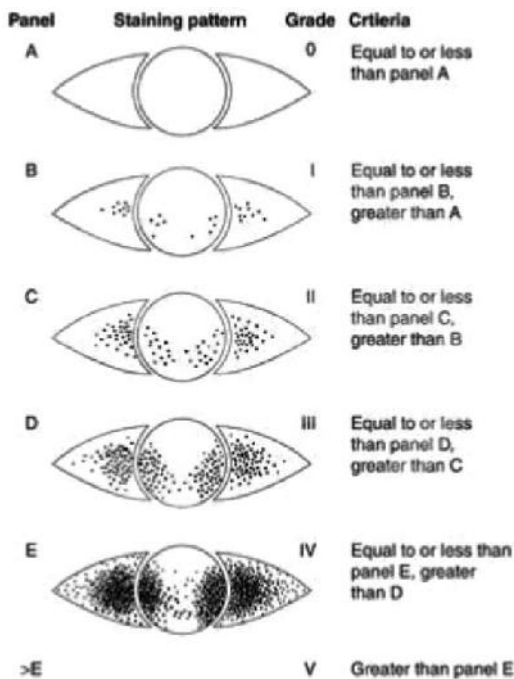
While staining both eyes with Rose Bengal stain and grading it with Oxford classification we observed that in control group only 5 patients showed a positive staining in right eye and only 2 patients in left eye. But in diabetic group 14 patients showed staining in right eye and 13 patients showed staining in left eye. (FIG VII)A significant difference staining test result was seen for left eye.Chi-square test used for the analysis which showed a non significant value in right eye (p=0.098) but a significant value in left eye (p=0.0276). This test could not be considered reliable for analysis of both groups. 8 control patients had dry eyes in right eye and 5 had dry eyes in left eyes.

According to DEWS severity grading in diabetic group 36 patients had dry eyes in right eye and 31 had dry eyes in left eye. In the diabetic group 13 patients had grade 1 dry eye, 20 had grade 2 and 3 had grade 3 dry eyes in right eye and 9 patients had grade 1 dry eye , 19 had grade 2 and 3 had grade 3 dry eyes in left eye. No patient showed grade 4 dry eye.(FIG VIII) 37 patients in diabetic age group showed dry eyes which means 49% patients had dry eyes.(FIG IX)

**SECONDARY OUTCOMES :**

As per DEWS severity grading ,the patients analysed as having dry eyes were correlated with various other outcomes.

**PHOTO I - Oxfords grading for rose Bengal staining**

| Panel | Staining pattern | Grade | Criteria |
|---|---|---|---|
| A | | 0 | Equal to or less than panel A |
| B | | I | Equal to or less than panel B, greater than A |
| C | | II | Equal to or less than panel C, greater than B |
| D | | III | Equal to or less than panel D, greater than C |
| E | | IV | Equal to or less than panel E, greater than D |
| >E | | V | Greater than panel E |

1) CORRELATION OF DRY EYES WITH GENDER :

Out of 37 diabetic patients who had dry eyes 20 were males (54%) and 17 were females (46%) which means males were more.But the correlation was not statistically significant(chi-square test,p=0.333). This means gender did not have any association with dry eyes.

2) CORRELATION OF DRY EYES WITH AGE :

There were 7 (44%) patients with dry eyes in 41-50 years , 13 (48%) in 51-60 years and 17 (53%) in 61-70 years. This shows that dry eye occurance increases with increasing age in diabetic patients. This may also be due to the increases duration of diabetes with increasing age.

But statistically the data was not significant (chi-square,p=0.398)

3) CO-RELATION OF DRY EYES AND YEARS OF DIABETES:

As per DEWS classification ,the patients analysed as having dry eyes were correlated with the duration of diabetes.

With increasing age the percentage of patients with dry eyes in that age group.We can see that in patients with more than 7 years of diabetes more 50% patients in that age group had dry eyes with 100% in 10 years duration(TABLE II).But this data was statistically not significant (p>0.05), which may be due to small sample size.

4) CORRELATION BETWEEN DIABETIC RETINOPATHY AND DRY EYES :

Out of 75 diabetic patients 54 had a normal fundus and 21 patients had diabetic retinopathy. And out of the 21 patients with diabetic retinopathy 14 patients had dry eyes meaning 67 %(FIG X). This means that with presence of diabetic retinopathy, dry eyes could also be a possible association in diabetic patients. Though statistic test didn't show a positive correlation p value 0.075 which may be due to small sample size, but 67 % patients with diabetic retinopathy showed dry eyes.

We observed severely reduced readings in patients who had severe Non-Proliferative diabetic retinopathy (NPDR) and Proliferative dibateic retinopathy (PDR).

**PHOTO II : DEWS severity grading of dry eyes.**

| Dry Eye Severity Level | 1 | 2 | 3 | 4* |
|---|---|---|---|---|
| Discomfort, severity & frequency | Mild and/or episodic; occurs under environmental stress | Moderate episodic or chronic, stress or no stress | Severe frequent or constant without stress | Severe and/or disabling and constant |
| Visual symptoms | None or episodic mild fatigue | Annoying and/or activity-limiting episodic | Annoying, chronic and/or constant, limiting activity | Constant and/or possibly disabling |
| Conjunctival injection | None to mild | None to mild | +/- | +/++ |
| Conjunctival staining | None to mild | Variable | Moderate to marked | Marked |
| Corneal staining (severity/location) | None to mild | Variable | Marked central | Severe punctate erosions |
| Corneal/tear signs | None to mild | Mild debris, ↓ meniscus | Filamentary keratitis, mucus clumping, ↑ tear debris | Filamentary keratitis, mucus clumping, ↑ tear debris, ulceration |
| Lid/meibomian glands | MGD variably present | MGD variably present | Frequent | Trichiasis, keratinization, symblepharon |
| TFBUT (sec) | Variable | ≤10 | ≤5 | Immediate |
| Schirmer score (mm/5 min) | Variable | ≤10 | ≤5 | ≤2 |

*Must have signs AND symptoms. TBUT: fluorescein tear break-up time. MGD: meibomian gland disease
Reprinted with permission from Behrens A, Doyle JJ, Stern L, et al. Dysfunctional tear syndrome. A Delphi approach to treatment recommendations. Cornea 2006;25:90-7

## DISCUSSION

In our study we compared and correlated the tear film tests in control and diabetic groups.

A total of 150 patients were observed for both eyes out of which 75 were diabetic and 75 non diabetic.

Mean age of patients in our study for control was 57.89±7.21 years and mean age in diabetics was 57.49±7.54 years. Maximum patients were in the age group 61-70 years followed by 51-60 years followed by 41-50 years

There were more males than females in the study

We compared tear film tests in both groups like schirmer's test, tear film break up time, tear meniscus height ,Rose Bengal staining and results showed significantly reduced values in diabetic than in controls.

Shirmer's test showed significantly different results of 23.49±7.98 mm vs 17.19±9.54mm, p <0.0001 for right eye and 24.8±7mm.66 vs 18.44±10.5mm, p =0.0001 for left eye.

TBUT also showed a significantly different result in both groups as for right eye 11.9±2.07 seconds vs 9.16±3.37 seconds ,p<0.001 for right eye and 11.97±2.01 seconds vs 9.50±3.10 seconds,p>0.0001 for left eye.

Tear meniscus height showed significantly different result for both groups of 0.81±.026 mm vs 0.56±0.32 mm,p<0.0001 for right eye and 0.79±.023 mm vs 0.57±.032 mm ,p<0.0001 for left eye.

Rose Bengal staining didn't show much significant result for right eye but was significant for left eye. It did not give a reliable result.

Also these studies showed significant correlation between dry eyes and diabetic retinopathy.

On correlating the data in our study ,gender did not affect the number of patients with dry eyes.Age wise distribution did not show a statistic significance but on calculating percentage we could infer that patients in age group of 61-70 years had more dry eyes and that older age can be a factor for dry eye in diabetic patients.Also percentage calculation showed that with increasing duration of diabetes the number of dry eyes increased.And on correlating with diabetic retinopathy dry eyes were common in patients having diabetic retinopathy. Though statistically the results are not significant for secondary outcome percentage calculation is significant.This may be due the small size of the sample.

Similar to our study , a study conducted by Kersewani et al[11] showed reduced values of schirmer's test ( patients with diabetic retinopathy 9.54±5.32 mm vs ,Diabetic 9.95±4.56 mm vs Control25.84±7.32 mm ) and tear film break up time (patients with diabetic retinopathy 7.90±2.36 s vs diabetic  9.65±2.87 s vs Control 14.54±2.92 s ).

Another study conducted by Pai Shobha et al [12] also showed reduced values of tear film tests.( 13.4±5.7 mm vs  7.7±3.9 mm for schirmer's test and  12.8±5.71vs 9.8±7.01sec for tear film break up time).

In our study few patients had a normal schirmer's test but abnormal other tests,this may be due to reflex secretion while doing the test.These patients got included in dry eye count in other tests but not for schirmer's test. So we observed that there was no ideal test to find out dry eyes and we cannot rely only on shirmer's test for screening and diagnosis and other tests should also be performed along with schirmer's test.

## CONCLUSION

Our study shows that diabetes affects the tear film production and tear film test were reduced in diabetic patients as compared to control group. So, it is important that diabetic patients be examined for tear film along with routine fundus examination. The severity of dry eye correlates to tear film secretion and volume as demonstrated by decreased Schirmer's test result, TBUT and tear meniscus height. Schirmer's test and Tear film break up time tests should be routinely done for diabetic patients and especially those with symptoms. Rose Bengal test was not found to be significantly different among the two groups in our study.

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