Comparative Study of the Pre-Corneal Tear Film in Diabetic and Non Diabetic Patients

Purva Agarwal¹, Ramya Krishna², Jonnadula Aravind³

1, 2, 3rd YR Postgraduate Ophthalmology

Abstract: Diabetes mellitus may induce various kinds of ocular complications. It is well known that diabetes induces retinopathy and cataract, but recently it is being increasingly recognized, that the tear film is also adversely affected in diabetics. Examination of 400 eyes of an equal number of diabetics and non-diabetics revealed that after age and gender adjustment, there was a significantly higher percentage of diabetic patients (19%) who had Dry Eye Disorder, compared with non-diabetic patients (7%, P < .001). This difference was significant for all age groups and for both sexes (P < .001), and it was also significantly related to outdoor occupations. Additionally, there was a positive correlation between diabetic retinopathy, decreased corneal sensation and dry eye syndrome especially when associated with poor glycemic control. This study shows that dry eye syndrome is an important manifestation of diabetes mellitus and highlights the fact that Tear film function and ocular surface evaluation must be included in the routine examination protocol for all diabetics.

Keywords: Tear film function, Dry eye, Diabetes mellitus, Diabetic retinopathy

1. Introduction

The importance of the cornea lies in its ability to refract rays of light at the air-cornea interface and to allow passage of these rays into the eye. Thus, corneal transparency is vital to the ability to see. Transparency is aided by the presence of a pre-corneal tear film which keeps the corneal surface in a moist state.

The pre-corneal tear film is composed of three intertwining layers, an outer lipid layer, a middle aqueous layer, also known as the hydrated gel layer, and an inner mucin layer. Tears are produced shortly after birth and their production increases considerably during the neonatal period while excess reflex tearing starts only after four months of age possibly due to the low innervation of the cornea in the very young.[1] Tears are drained out of the eye, via the nasolacrimal passages, into the inferior meatus of the nose.[2] Effective resurfacing of the tear film is dependent on the presence of a normal blink reflex, proper contact between the external ocular surface and eyelids, and the presence of normal corneal epithelium.[3]

In the absence of a normal pre-corneal tear film, the cornea tends to dry out and becomes hazy, leading to a condition of dry eye. Dry Eye is a fairly common clinical entity which tends to affect between 5% to 28% adults, among the general population globally.[4] It has been estimated that about 3.23 million women and 1.68 million men 50years or older have dry eye.[5,6]

Several local and systemic disorders predispose the eye to the development of dry eye, one among them being diabetes mellitus. While diabetic retinopathy is the more commonly known ocular complication of diabetes, diabetic patients have also been found to have symptoms indicative of dry eye such as foreign body and burning sensations, itching, blurred vision, and photophobia, stinging, dryness, ocular fatigue and redness. There is, thus, an implication of a correlation between diabetes mellitus and tear film abnormalities.

This study highlights the need for careful attention to a patient’s complaints and to diligently look for signs of dry eye in all diabetic patients.

Aims & Objectives
1) To determine the characteristics of the pre-corneal tear film in eyes of diabetic individuals.
2) To compare the pre-corneal tear film in eyes of diabetic and non-diabetic individuals

2. Materials & Methods

This prospective non randomized study was conducted at Santiram Medical College And General Hospital during the period August 2018 to July 2019. 200 participants were enrolled from among individuals reporting to the Ophthalmology OutPatient Department of Santhiram Medical College And General Hospital, Nandyal. Participants were assigned to age and gender matched groups after obtaining written consent.

Inclusion criteria
1) Known diabetic patients
2) Non diabetic patients as control group

Exclusion criteria
1) Patients with any ocular disorder known to produce dryeye.
2) Patients suffering from any systemic diseases, (other than diabetes mellitus), associated with dry eye such as connective tissue disorders (Sjogren's syndrome, Rheumatoid arthritis, Lupuserythromatosis).
3) Patients on any drug treatment which produces dry eye (such as MAO inhibitors, Alpha agonists, Beta blockers, Thiazides etc)
4) Patients having undergone any ocular surgery in the past 2years
5) Wearers of contact lenses
2.1 Methodology

A detailed history, general physical examination, detailed ophthalmologic examination and relevant investigations were recorded for each patient enrolled in the study. Data was captured on a standard proforma. In addition to determining blood sugar levels, the following tests were performed.

1) **Corneal sensitivity test:** Corneal sensitivity was tested using a wisp of cotton brought onto the cornea in order to elicit a blink response. Presence of a brisk blink response was indicative of normal corneal sensation. Presence of a weak blink response was indicative of reduced corneal sensation. An absent blink response indicated absence of corneal sensation.

2) **Tear film Break up Time (TBUT):** The tear film was stained using commercially available pre-sterilized strip impregnated with 1mg Fluorescein. The tear film was stained in an un-anesthetized eye. The patient was instructed to blink once or twice and then stare straight ahead without blinking while the cornea was scanned under low slit lamp magnification using a blue cobalt filter. The end point of the test occurred with the time taken, in seconds, for the appearance of the first dry spot formation from the last blink.

3) **Schirmer’s test:** This test was performed using a commercial Whatman41 paper strip. The strip was placed at the junction of the middle and lateral thirds of the lower eyelid and removed after 5 minutes. The amount of wetting of the strip was read off in millimetres.

4) **Dye tests:** The following dye tests were also carried out and grading of the corneal and conjunctival staining was done based on the grading system of the National Eye Institute (NEI) industry Workshop on Clinical Trials in Dry Eyes.

5) **Fluorescein staining:** A commercially available Fluorescein impregnated strip was introduced into the inferior conjunctival sac temporal. The patient was asked to gently close and roll the eyes around to adequately distribute the dye across the ocular surface. Each eye was then examined through the slit lamp using a cobalt blue filter and any areas of staining of the corneal surface were noted.

6) **Lissamine green strip:** A strip impregnated with lissamine green was used as above to detect areas of mucin deficiency in the ocular surface using a red barrier filter.

7) **Rose Bengal staining:** A moistened commercial strip impregnated with 1.5mg Rose Bengal was applied to the inferior cul-de-sac, without anesthesia. The eye was examined with the slit lamp using a green filter.

3. Results

400 eyes of 200 patients were examined in this non-randomized prospective study. The participants were divided into 2 groups, Group A comprising of 100 non diabetic individuals and the other group (Group B), comprised of 100 known diabetics participants. Group A was taken as the control group.

Of the total of 200 participants, 86 were males and 114 were females. 53% participants had an outdoor occupation and had a greater frequency of dry eye disorder than those with indoor occupations. Six (5.66%) individuals of group A, with outdoor occupations had DED while 12 (11.32%) individuals in group B, had DED. The influence of outdoor occupation on development of DED is statistically significant with p=0.006. Symptoms were non specific, mainly itching, burning of eyes and foreign body sensation. However, diabetics had fewer symptoms than their non diabetic counterparts. TBUT test was positive in 18 eyes (9%) belonging to the non-diabetic group and 38 eyes (19%) in the diabetic group. Positive Schirmer’s tests were seen in 7% of non diabetics and 24% of diabetics. (P = 0.01). Fluorescein staining was positive in 19% of diabetic individuals as compared to 4% of non-diabetics. All affected eyes showed NEI grading of 3.

3% of the non diabetic group A as well as 19% of the diabetic group B had graded 3 Rose Bengal staining. 38 eyes (19%) of Group B individuals had grade 3 positive areas of mucin deficient conjunctiva on staining with Lissamine green showed 19% prevalence of DED was present in Group B diabetic patients with a significantly higher percentage occurring in those with longer duration of diabetes.
Age and gender distribution in group A (non diabetic)

**Occupation:** In group A, 33 males and 21 females followed an outdoor occupation while 9 males and 37 females spent most of their time indoors.

**Dry eye and occupation** the influence of outdoor occupation on development of DED is statistically significant with \( p = 0.006 \)

Duration of diabetes according to age and gender

<table>
<thead>
<tr>
<th>Age Group</th>
<th>40-45 yrs</th>
<th>46-50 yrs</th>
<th>51-55 yrs</th>
<th>56-60 yrs</th>
<th>61-65 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>M</td>
<td>F</td>
<td>M</td>
<td>F</td>
<td>M</td>
</tr>
<tr>
<td>&lt;5 yrs</td>
<td>6</td>
<td>9</td>
<td>6</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>6 yrs-10 yrs</td>
<td>4</td>
<td>5</td>
<td>10</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>11 yrs-15 yrs</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>&gt;15 yrs</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

**Duration DM**

<table>
<thead>
<tr>
<th>Duration</th>
<th>DM Dry eye</th>
<th>No dry eye</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5 yrs</td>
<td>0</td>
<td>44</td>
<td>44</td>
</tr>
<tr>
<td>5 yrs-10 yrs</td>
<td>8</td>
<td>31</td>
<td>39</td>
</tr>
<tr>
<td>10 yrs-15 yrs</td>
<td>9</td>
<td>6</td>
<td>15</td>
</tr>
<tr>
<td>&gt;15 yrs</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
<td>81</td>
<td>100%</td>
</tr>
</tbody>
</table>
34 eyes (18.5%) of diabetic patients showed presence of non-proliferative diabetic retinopathy. Only 1 eye showed the presence of proliferative diabetic retinopathy.
Corneal sensation group Cross tabulation

<table>
<thead>
<tr>
<th>Corneal Sensation</th>
<th>Normal</th>
<th>Abnormal</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>81</td>
<td>19</td>
<td>100</td>
</tr>
<tr>
<td>Non Diabetes Mellitus</td>
<td>93</td>
<td>7</td>
<td>100</td>
</tr>
<tr>
<td>Total</td>
<td>174</td>
<td>26</td>
<td>200</td>
</tr>
<tr>
<td>% within Corneal Sensation</td>
<td>46.6%</td>
<td>73.1%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Positive test results - Group A

<table>
<thead>
<tr>
<th>Age Group</th>
<th>40-45 yrs</th>
<th>46-50 yrs</th>
<th>51-55 yrs</th>
<th>56-60 yrs</th>
<th>61-65 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test</td>
<td>M</td>
<td>F</td>
<td>M</td>
<td>F</td>
<td>M</td>
</tr>
<tr>
<td>BUT</td>
<td></td>
<td></td>
<td>1</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Schirmer’s test I</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Flourescein staining</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rose Bengal staining</td>
<td>1</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lissamine green staining</td>
<td>1</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Test results of diabetic group age wise: Investigation tests of the pre-corneal tear film in the diabetic group were positive for the following tests: Schirmer’s in forty eight (24 %) eyes, Tear BUT test in 38 eyes (19%), Rose Bengal test together with Lissamine green in thirty eight eyes (19 %)
4. Discussion

This hospital based study was done on 400 eyes of 100 normal individuals (Group A) and 100 diabetics (Group B). There were a total of 86 males and 114 females in the study. The youngest participant was a female aged 40 years and the oldest was a 65 years old male. The mean age of all participants was 50.31 years. The mean age of the men was 50.13 years and the mean age of the women was 50.27 years.

Of the total of 200 participants, 53% participants, (70 males and 36 females) had an outdoor occupation while (16 males and 78 females) followed largely indoor occupations. 54 participants (33 males and 21 females) of Group A and 52 participants (37 males and 15 females) of Group B had an outdoor occupation. Those with indoor occupations were 46 participants (9 males and 37 females) from Group A and 48 participants (7 males and 41 females) from Group B. Environmental exposure is thought to play a role in the development of DED.

In this series, group A, six individuals, i.e.3 Males & 3 Females, with outdoor occupations had DED while in group B 12 individuals, i.e.10 males & 2 females, had DED. The influence of outdoor occupation on development of DED is statistically significant with p=0.006

Individuals belonging to group B had been suffering from diabetes mellitus for periods varying from 2 years to 17 years. The mean duration of diabetes was 6.8years. It is well known that diabetic changes in the retina are duration dependent, and diabetics with over ten years of the disease will start to develop retinopathy. The severity of retinopathy is influenced by the state of control of the diabetes.[3,6] 51% (26 males and 25 females) of individuals had a good control of diabetes while 12% (3 males and 9 females) had poor control of their blood sugar levels. Diabetic retinopathy had affected 36(18%) eyes of 9 males and 9 females.

In the present study, DED was found to affect a total of 52 eyes representing 13% of the eyes in the study. 23 out of the 26 affected individuals were above 50 years of age and 3 were below 50 years of age. Seven non diabetics with DED were above 55 years of age, while 19 diabetics had developed DED at a younger age. Women are affected twice as often as men. 5,6 Moss and associates, 39 too, reported a higher incidence of dry eye among females, 16.7% compared to 11.4% in males, but this difference tends to occur only in the older age groups.[8] Dry eyes were detected in total of 5 males and 11 females. In this series no patient was older than 65 years.

The prevalence of DED is significantly higher in diabetic individuals, affecting 20% to 37% of all diabetics.[9] Seifart and associates reported that this was due to loss of conjunctival goblet cells, decreased corneal sensitivity and neuropathy involving the lacrimal glands. The incidence of DED is higher with longer durations of diabetes.

Along with a higher age related incidence the severity of symptoms is also found to be greater amongst older people. The symptoms are non specific and consist mainly of itching, burning of eyes, and foreign body sensation. 33 individuals presented with complaints of itching, 31 reported with ocular foreign body sensations and 20 complained of a burning sensation in their eyes.

Tear film adequacy as tested by Schirmer’s test shows considerably lesser wetting of the strip in DED.[10] Positive Schirmer’s tests were seen in 14 eyes of non diabetics and 48 eyes of diabetics. There were significantly lower values amongst diabetics with DED. Fluorescein staining was positive in 38 eyes of diabetic patients as compared to 8 eyes of non-diabetics. NEI grading of the corneal staining is taken to be positive if the score is 3 or more. All the eyes showed NEI grading of 3. There were no eyes with higher NEI grading.

Rose Bengal testing is done to detect the presence of dead and devitalized epithelial cells. 6 eyes of non diabetic group (Group A) as well as 38 eyes in group B had grade 3 Rose Bengal staining.

Lissamine green staining for detection of mucin deficient conjunctival areas showed grade 3 positive results in 38 eyes of Group B individuals.

All these findings strongly suggest that dry eye is a significant feature of the diabetic ocular surface disease. Schirmer’s test results were significantly positive in diabetic individuals (p=0.01) and were also significantly lower in those with poor metabolic control.

5. Conclusion

This study shows that dry eye syndrome is an important manifestation of diabetes mellitus. It develops at an earlier age in diabetics, and both the duration of diabetes and the stage of retinopathy correlate well with the occurrence and severity of tear film dysfunction. DED is easily detected and monitored by performing simple non invasive testing of the tear film and should be a part of routine check up at each ophthalmic visit, even if the patient is asymptomatic. Early diagnosis and timely treatment are important for preventing development of DED and its subsequent progression to vision threatening complications and to improve the quality of life.

References


Author Profile

Dr. Purva Agarwal, 3rd year postgraduate, Ophthalmology, Santiram Medical College and General Hospital, Nandyal, Born and brought up in Hyderabad.

Dr. TG Ramya Krishna, 3rd year Postgraduate Ophthalmology, Santiram Medical College and General Hospital, Nandyal, Born and brought up in Tirupathi.

Dr. Jonnadulu Aravind, 3rd year postgraduate ophthalmology, Santiram Medical College and General Hospital, Nandyal. Born and brought up in Rajampeta.