Dry Eye in Patients With Diabetic Retinopathy: A Clinical Study

Geetika Khurana1, Deeksha Khurana1, Rajesh Jain3

1Department of Ophthalmology Army College of Medical Sciences & Base Hospital Delhi Cantt, India
2Maulana Azad Medical College & Associated hospitals, New Delhi, India
3Department of Ophthalmology Lady Hardinge Medical College & Associated hospitals, New Delhi, India

Abstract

Purpose: To study tear film changes in patients of Type 2 diabetes mellitus with and without diabetic retinopathy.

Method: A hospital based, cross sectional, observational study including 40 patients of Type 2 diabetes mellitus with diabetic retinopathy and 40 patients without diabetic retinopathy. The parameters evaluated for each patient included a questionnaire (based on McMonnie’s Dry Eye questionnaire), Schirmer’s basic secretion test (BST) and Tear film break up time (TBUT).

Results: The prevalence of dry eye in patients without diabetic retinopathy was 5% (Schirmer’s BST) and 42.5% (TBUT) as compared to 21.25% (Schirmer’s BST) and 82.5% (TBUT) in patients with diabetic retinopathy. Schirmer’s BST and TBUT were found decreased with the increase in severity of diabetic retinopathy (p<0.001).

Conclusions: The prevalence and severity of dry eye, based on clinical parameters, was more in patients with diabetic retinopathy as compared to those without diabetic retinopathy.

Keywords: dry eye, diabetic retinopathy, schirmer’s BST, TBUT

Introduction

Dry eye is a disorder of the precorneal tear film due to tear deficiency or excessive evaporation which causes damage to the interpalpebral ocular surface and is associated with symptoms of ocular discomfort. Around 5% of urban Indian population suffers from Type 2 diabetes mellitus.1,2 Approximately 370 million people across the world are expected to be affected by diabetes by the year 2030.3 According to an Indian study by Khurana et al4, dry eye is incident among 0.46% of ophthalmology outpatients in India. A hospital based study conducted at New Delhi showed the overall prevalence of dry eye in patients attending Ophthalmology OPD based on Ocular Surface Disease Index to be 29.25% in patients over 40 years of age.5 The prevalence of diabetic retinopathy in Indian urban population with diabetes mellitus was found to be 18%.6 The manifestations of ocular surface disease in diabetes include defect in tear film quantity and quality, goblet cell loss, higher grade of squamous metaplasia and reduced corneal sensation which are affected by status of metabolic control and peripheral neuropathy. The presence of retinopathy in diabetes is often accompanied by other complications including nephropathy and neuropathy. However, the relationship between diabetic retinopathy and ocular surface disorders has not been well described in the literature.

Material And Methods

The study was conducted in Lady Hardinge Medical College and Smt Sucheta Kriplani Hospital, New Delhi, India in the Departments of Ophthalmology and Pathology.

Inclusion Criteria

All cases of Type 2 diabetes mellitus with age ≥ 40 years with and without diabetic retinopathy attending the Ophthalmology OPD over the period Nov 2012 – Mar 2014 were considered for the study. The study subjects were divided into two groups. Group A consisted of patients of Type 2 diabetes mellitus with clinical evidence of diabetic retinopathy. Group B consisted of patients of Type 2 diabetes mellitus without clinical evidence of diabetic retinopathy. 40 patients (80 eyes) were enrolled in each of the above two groups after obtaining a written informed consent.

Exclusion Criteria

The patients excluded from the study were any patients with history of current or recent use of topical/systemic ocular medication like beta blockers, diuretics, anticholinergics, anti-histaminics, tricyclic antidepressants, lubricants that could cause/affect dry eye condition; history or clinical evidence of any ocular disorders like blepharitis, lid deformities that could possibly interfere with the interpretation of study result; recent ocular surgery or trauma of any kind, including chemical trauma; other systemic/autoimmune diseases like Sjogren’s syndrome, rheumatoid arthritis, lupus; known to affect the ocular surface; contact lens wearers, patients having undergone LASIK surgery; pregnant/lactating females; cigarette smokers; patients with clinical evidence of Vitamin A deficiency and eyes in which clinical fundus examination was not possible. A cross-sectional evaluation was conducted and all patients were subjected to detailed clinical work up, including McMonnie’s questionnaire and tear film studies. A detailed clinical history including symptoms of dry eye, occupational
and medication history, other predisposing risk factors for dry eye, duration of diabetes etc was elicited from all patients enrolled in the study. McMonnie’s dry eye questionnaire was answered by all the subjects and appropriate scoring was done.

Detailed general physical examination and systemic clinical examination was done for all subjects to exclude the presence of collagen vascular or mucocutaneous disorders. Ocular Examination included evaluation of Visual acuity, Eyelids (to look for blepharitis, trichiasis, meibomitis, ectropion, hordeolum etc.), Conjunctiva (to look for congestion, follicles, papillae, tortuosity of vessels, symblepharon etc.), Lacrimal apparatus (position and patency of punctum and further drainage system, tear film tests), Cornea (surface contour, loss of normal lustre, filaments, vascularization, keratic precipitates), Anterior chamber, Posterior segment (fundus examination using direct and indirect ophthalmoscope and +90 D lens). Presence or absence of diabetic retinopathy was looked for and graded as proliferative or non-proliferative, if present. For tear film evaluation, Tear film break up time (TBUT), Fluorescein staining and Schirmer basic secretion test (BST) were done. An average of values for the 2 eyes was used for statistical analysis. Tear film break up time is defined as the time, in seconds, between the last blink and the appearance of the first random dry spot on the cornea. The lower fornix was stained using a presterilized strip of 2% fluorescein. The patient looked straight without blinking while seated on a slit lamp and was observed using the broad beam of cobalt blue light. The time taken for the appearance of first random dark spot was noted. TBUT of less than 10 seconds was considered abnormal.

For fluorescein staining, a commercially available presterilized strip of 2% fluorescein was inserted into the lower fornix of each eye. After several blinks which ensured even spread of the stain, the staining pattern of the ocular surface was observed under cobalt blue light of the slit lamp. Both interpalpebral conjunctival and corneal staining was recorded as being present or absent. For Schirmer’s basic secretion test, Proparacaine 0.5% (preservative free) drops were instilled into the conjunctival sac, following which the basal tear secretion was estimated. A strip of commercially available presterilized Whatman filter paper measuring 5 x 35 mm was taken, folded into the lower fornix at the junction of the middle and lateral third of the lid margin. The amount of wetting of the paper was recorded in mm at the end of 5 minutes. Any value less than 10 mm was taken as an indicator of dry eye. The data was analyzed using SPSS version 20.0. The comparison of continuous variables between and within the groups was done using student’s t-test, while the discrete data was compared using chi-square test. The confidence limit for significance was fixed at 95% level with p-value < 0.05.

Results

The mean age of the patients enrolled in this study was 57.02 ± 9.37 years, the minimum being 40 years and the maximum being 80 years. Out of the 80 diabetic patients enrolled for the study, 34 (42.5%) were males and 46 (57.5%) were females. Out of the 34 males enrolled for the study, 14 (41.18%) had evidence of diabetic retinopathy while 20 (58.82%) had no evidence of diabetic retinopathy. Out of the 46 females enrolled, 26 (56.52%) showed evidence of diabetic retinopathy while 20 (43.48%) had no evidence of the same. The presence of various symptoms of dry eye disorder were noted and scored according to the McMonnie’s Dry Eye Questionnaire (Figure 1). Foreign body sensation was the most common reported symptom and itching was the least reported symptom. All symptoms of dry eye, except itching, were found to be higher in patients with diabetic retinopathy as compared to patients without diabetic retinopathy (Table 1). All signs of dry eye disorder were significantly more common in patients with diabetic retinopathy as compared to those without diabetic retinopathy (Table 2, 3) (p<0.0001).

Tortuosity of conjunctival vessels was seen in 100% (21 of 21) patients with dry eye diagnosed by Schirmer test and 66% (33 of 50) patients with dry eye diagnosed by TBUT. Decreased corneal luster was seen in 80.95% (17 of 21) patients with dry eye diagnosed by Schirmer test and 42% (21 of 50) patients with dry eye diagnosed by TBUT. Fluorescein staining of conjunctiva and cornea was seen in 28.57% (6 of 21) patients of dry eye diagnosed by Schirmer test and 20% (10 of 50) patients with dry eye diagnosed by TBUT.

Table 1: Symptoms of dry eye in patients with and without diabetic retinopathy.

| SYMPTOMS | Overall | With Retinopathy | Without Retinopathy |
|----------|---------|-----------------|---------------------|
| Foreign body sensation | N (%) | n (%) | N (%) |
| Grittiness | 57 | 71.5 | 37 | 46.3 | 20 | 25.0 |
| Burning sensation | 37 | 46.3 | 26 | 33.5 | 11 | 13.8 |
| Itching | 14 | 17.5 | 6 | 7.5 | 8 | 10.0 |
| Dryness | 67 | 83.0 | 37 | 46.3 | 30 | 37.5 |
| Effect of indirect exposure to cigarette smoke, smog, AC, central heating on eyes | 17 | 21.3 | 11 | 13.8 | 6 | 7.5 |
| Feeling of dryness of eyes after alcohol intake | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Joint pain | 2 | 2.5 | 2 | 2.5 | 0 | 0.0 |
| Dryness of nose, mouth, throat | 4 | 5.0 | 0 | 0.0 | 4 | 5.0 |
| Known thyroid abnormality | 2 | 2.5 | 2 | 2.5 | 0 | 0.0 |
| Whether known to sleep with eyes open | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Eye irritation on waking | 46 | 57.5 | 36 | 45.0 | 10 | 12.5 |

Table 2: Clinical signs of dry eye in patients with and without diabetic retinopathy

| Signs | Overall | With Retinopathy | Without retinopathy |
|-------|---------|-----------------|---------------------|
| Conjunctival Vascular Tortuosity | 29.4% | 60.8% | 70.0% | 6 | 22 | 25% | 4 | 6 |
| Decreased Normal Corneal Luster | 23.5% | 28.2% | 47.5% | 6 | 13 | 5% | 2 | 0 |
| Fluorescein Staining | 5.8% | 17.3% | 20% | 0 | 8 | 5% | 2 | 0 |
Our >45 age group was reported that Schirmer mean Schirmer’s value in the patients in the group with diabetic retinopathy. However, the eye was lower in patients without diabetic retinopathy. Therefore, mean Schirmer’s value in patients with dry eye. Among patients without diabetic retinopathy, be 14.23±2.84mm while it was 6.70±1.68mm in those with diabetic retinopathy. Among patients with diabetic retinopathy, the mean Schirmer’s value ≤10mm (p<0.0001). Patients with diabetic retinopathy had 6.65 times more chance of having Schirmer’s BST value ≤10mm than those without diabetic retinopathy. 82.5% of the patients (33 patients) with diabetic retinopathy were recorded to be having TBUT≤10 seconds. 42.5% of the patients (17 patients) without diabetic retinopathy were recorded to be having TBUT≤10 seconds (Table 4). The mean TBUT in patients without diabetic retinopathy was 9.8±2.19 seconds as compared to 6.97±2.01 in those with diabetic retinopathy. Among the patients with dry eye, the mean TBUT in those without diabetic retinopathy was 7.88±1.45 seconds as compared to 6.33±1.59 in those with diabetic retinopathy (p<0.001). Patients with diabetic retinopathy had 6.37 times more chance of having TBUT≤10 seconds than those without diabetic retinopathy.

**Discussion**

Various studies have previously reported increased incidence of dry eye syndrome in diabetic patients. A study by Seifart et al showed that 52.8% of all diabetic subjects complained of dry eye symptoms, as against 9.3% of the controls. They concluded that close monitoring of diabetic patients and good blood sugar regulation is important for the prevention of dry eye syndrome and retinopathy. Our study found a higher prevalence of dry eye disorder in diabetic patients. High prevalence of dry eye disorder can be explained by low tear production DM patients related to dysfunction of the autonomic nervous system. The tropical and dry climate of our region could be the reason for high prevalence of dry eye seen in our study. Jin et al reported that TBUT is significantly lower in type 2 diabetic patients as compared to controls while Goebels reported that Schirmer test and tearing reflex was significantly lower in diabetic patients compared with control group. We found abnormal Schirmer’s test in 26.25% of patients with abnormal TBUT in 62.50% patients. Manaviat et al concluded that 59.3% of patients with diabetic retinopathy suffered from dry eye syndrome which was higher than patients without diabetic retinopathy. Dogru et al also reported that TBUT and Schirmer test values are significantly lower in the diabetic patients, especially in patients with peripheral neuropathy and poor metabolic control. Deterioration of tear film status was found to be significantly associated with severity of diabetic retinopathy by Ozdemir et al. Our study found similar results showing that the patients with diabetic retinopathy had a 6.65 times more chance of having Schirmer’s BST value ≤10mm than those without diabetic retinopathy. Also, patients with diabetic retinopathy had 6.37 times more chance of having TBUT≤10 seconds than those without diabetic retinopathy. Presence of autonomic dysfunction, reduced corneal sensitivity, abnormalities of tear film dynamics, damage to the microvasculature of the lacrimal gland and subclinical meibomian gland dysfunction

| Scoring Scheme |  
|----------------|
| Male/Female |  
| Age | Score |  
|  
| Male | 25-45 | 4 |  
| Female | 25-45 | 3 |  
| Male | >45 | 2 |  
| Female | >45 | 6 |  

Score>20 is suggestive of dry eye while score between 10 and 20 is suggestive of borderline dry eye disease.

**Table 1: Mc Monnie’s Questionnaire for Dry eye**

| Schirmer’s ≤10mm | TBUT≤10 sec (with diabetic retinopathy) | TBUT≤10 sec (without diabetic retinopathy) |
|------------------|-----------------------------------------|-------------------------------------------|
| Gender           | Male/Female                             | Male/Female                              |
| Age              | 25-45                                   | >45                                       |
| Sex              | Male                                    | Female                                   |
| Score            | 6                                       | 15                                       |
|                  | 10                                      | 23                                       |
|                  | 6                                       | 11                                       |
|                  | 8                                       | 13                                       |
|                  | 2                                       | 4                                        |
|                  | 2                                       | 8                                        |
can all attribute to increased prevalence and severity of dry eye disorders in patients with diabetes. Lack of control group and glycemic parameters assessment especially HbA1C are limitations of our study. We have not evaluated and correlated the severity of diabetic retinopathy with severity of dry eye, and thus, we recommend further studies to evaluate the same.

**Conclusion**

Evaluation of diabetic patients for dry eye symptoms using a questionnaire is a good method of identifying dry eye in its early stages. Presence of diabetic retinopathy is an indicator of disease severity. Similar to the other ocular and systemic manifestations of diabetes mellitus, the presence and severity of dry eye syndrome was positively correlated with the presence of diabetic retinopathy in our study. Due to the multifactorial etiology and high prevalence of dry eye in patients with diabetes, we recommend that Diabetic clinics must include routine dry eye screening using questionnaires, Patients with diabetic retinopathy should be considered as being at higher risk for suffering from dry eye syndrome and Clinical evaluation for dry eye needs to be done in addition to routine fundus evaluation of diabetic patients, especially in those with evidence of diabetic retinopathy. Patients diagnosed with dry eye need suitable and adequate management of the same. Management of dry eye needs to be incorporated in the wholesome approach of treating a diabetic patient in addition to adequate glycemic control and management of diabetic retinopathy.

**References**

1. Mohan V, Shanthi Rani S, Deepa R, Premlatha G, Sastry NG, Saroja R. Intratrabor differences in the prevalence of the metabolic syndrome in southern India – The Chennai Urban Population Study. *Diabet Med* 2001; 18:280-87.

2. Ramachandran A, Snehitha C, Dharmaraj D, Viswanathan M. Prevalence of glucose intolerance in Asian Indians. Urban rural difference and significance of upper body adiposity. *Diabetes Care* 1992; 15:1348-55.

3. World Health Organization. Diabetes; Geneva; WHO media center [updated 2011 Aug; Cited 2012 Apr 15] Available from: http://www.who.int/mediacentre/factsheets/fs312/en/index.html/.

4. Khurana AK, Choudhary R, Ahluwalia BK, Gupta S. Hospital epidemiology of dry eye. Indian J Ophthalmol 1991; 39:55-8.

5. Gupta N, Prasad I, Jain R, D’Souza P. Estimating the prevalence of dry eye among Indian patients attending a tertiary ophthalmology clinic. *Ann Trop Med Parasitol* 2010; 104:247-55

6. Raman R, Rani PK, Reddi Rachepalle S, Gnanamoorthy P, Uthra S, Kumaranickavel G, Sharma T. Prevalence of diabetic retinopathy in India: Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetics Study report 2. *Ophthalmology* 2009; 116:311-8.

7. Manaviat MR, Rashidi M, Afkhami-ArkedaniM, Shoja MR. Prevalence of dry eye syndrome and diabetic retinopathy in type 2 diabetic patients. *BMC Ophthalmol* 2008; 8:10.

8. Seifart U, Strempel I. The dry eye syndrome and diabetes mellitus. *Ophthalmologe* 1994; 91:235-9.

9. Jin J, Chen LH, Liu XL, Jin GS, Lou SX, Fang FN: Tear film function in non insulin dependent diabetics. *Zhonghua Yan Ke Za Zhi* 2003; 39:10-3.

10. Goebbels M: Tear secretion and tear film function in insulin dependent diabetics. *Br J Ophthalmol* 2000; 84:19-21.

11. Dogru M, Katakami C, Inoue M. Tear function and ocular surface changes in noninsulin-dependent diabetes mellitus. *Ophthalmology* 2001; 108:586-92.

12. Ozdemir M, Buyukbese MA, Cetinkaya A, Ozdemir G. Risk factors for ocular surface disorders in patients with diabetes mellitus. *Diabetes Res Clin Pract* 2003; 59:195-99.