

## CORELATION OF DRY EYE STATUS WITH SEVERITY OF DIABETIC RETINOPATHY

Tanushree V<sup>1</sup>, H. T. Venkate Gowda<sup>2</sup>

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**ABSTRACT: AIM:** To study the correlation of dry eye status with severity of diabetic retinopathy. **MATERIALS AND METHODS: SETTINGS AND DESIGN:** Prospective study. One hundred patients with diabetes mellitus attending the outpatient and in-patient department, Department of Ophthalmology, K. R. Hospital, Mysore, were included under the study, between the periods from January 2014 to July 2014 (6 months). Informed and written consent was taken from all the patients. After detailed history, all necessary ocular and systemic examination was done. All diabetes mellitus patients were analyzed for dry eye status and presence of diabetic retinopathy changes. Dry eye status was evaluated with Schirmer's test, Tear film break up time and conjunctival impression cytology. Retinal status evaluation was done by direct ophthalmoscopy, indirect ophthalmoscopy and Slit lamp Biomicroscopy using 78D lens after pupillary dilation. Diabetic retinopathy was graded accordingly to ETDRS classification. **STATISTICAL ANALYSIS:** All data were analyzed using descriptive statistics and Chi square test and contingency coefficient analysis was applied. **RESULTS:** A total of 100 diabetes mellitus patients were analyzed. 56 (56%) patients had Diabetic retinopathy and 44(44%) had normal fundus picture. Out of the 100 diabetes mellitus patients, 36 (36%) patients had dry eye. Significant association (P – 0.001) between dry eye and diabetes mellitus was seen. **CONCLUSION:** Dry eye and diabetes mellitus have a common association. Dry eye is more frequent in diabetes mellitus patients with longer duration and in patients with Diabetic retinopathy. **KEYWORDS:** Dry eye, diabetic retinopathy, Tear film break up time, Schirmer's test.

**INTRODUCTION:** Diabetes is one of the most common leading causes of blindness.<sup>1</sup> The World Health Organization estimated that in 2002 diabetic retinopathy accounted for about 5% of world blindness, representing almost 5 million blind.

Cataract and retinopathy are well-known as ocular complications of diabetes. Recently, problems involving the ocular surface, dry eyes in particular have been reported in diabetic patients.<sup>1</sup> These patients suffer from a variety of corneal complications including superficial punctate keratopathy, trophic ulceration, and persistent epithelial defect.<sup>2</sup> Dry eye is an important contributor to these problems.

Dry eye is a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance and tears film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface.<sup>3</sup>

There are several theories that might explain the connection between dry eye and diabetes. The most frequently cited associated factors are:

- 1. Peripheral neuropathy secondary to hyperglycemia:** Hyperglycemia and microvascular damage to the corneal nerves can block the feedback mechanism that controls tear secretion.<sup>4</sup> When the innervation of the ocular surface is disrupted; the lacrimal gland does not secrete tears properly.

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- 2. Insulin insufficiency:** Corneal and lacrimal gland metabolism, growth, epithelial cell proliferation and culture maintenance are influenced by insulin.<sup>4</sup> A low insulin level generally disrupts the biomechanical balance of these tissues and results in ocular dryness.
- 3. Inflammation:** Hyperglycemia triggers inflammatory alterations and is believed to impair normal events, such as tear secretion.<sup>5</sup> Inflammation is not only a cause, but also a consequence of dry eye. Aqueous deficient dry eye or lacrimal insufficiency usually results from lacrimal gland inflammation.

Some of the ocular surface complications due to dry eye in diabetes are corneal and conjunctival epithelial alterations like punctate keratopathy, recurrent erosions, persistent epithelial defects, neurotrophic keratopathy, wound healing delay, higher risk of microbial keratitis and potential visual impairment due to corneal scarring

Therefore early diagnosis of dry eye syndrome in diabetic patients is important for beginning of treatment in early stages.

**AIMS AND OBJECTIVES OF THE STUDY:** To correlate dry eye status with the severity of Diabetic retinopathy.

**MATERIALS AND METHODS: SOURCE OF DATA:** One hundred patients with diabetes mellitus attending the outpatient and in-patient department, Department of Ophthalmology, K. R. Hospital, Mysore, were included under the study, between the periods from January 2014 to July 2014 (6 months).

**SETTINGS AND DESIGN:** Prospective study.

**SAMPLE SIZE:** 100 patients.

**INCLUSION CRITERIA:** All diabetes mellitus patients, including new and review cases of diabetes (diagnosed according to ADA criteria).

**EXCLUSION CRITERIA:**

1. Patients on medications such as antihistamines, tricyclic antidepressants, oral contraceptives and diuretics.
2. Contact lens users.
3. Patient's undergone Lasik surgery.
4. Patient's having Sjogren's syndrome, Rheumatoid arthritis, Parkinson, Lupus.
5. Patients who are smokers.

**METHOD OF STUDY:** Informed and written consent was taken from all the patients.

A detailed history of each patient was obtained regarding the age, sex, ocular symptoms, and duration of diabetes mellitus and presence of other diseases. All necessary ocular and systemic examination was done. All diabetes mellitus patients were analyzed for dry eye status and presence of diabetic retinopathy changes.

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Dry eye was confirmed by ocular surface dye staining pattern with fluorescein, tear film break up time (value 15s), Schirmer's test (positive if 10mm or less in 5min) and conjunctival impression cytology. Diagnosis was established by positivity of one or more of the tests.

Retinal status evaluation was done by direct ophthalmoscopy, indirect ophthalmoscopy and Slit lamp Biomicroscopy using 78D lens after pupillary dilation. Diabetic retinopathy was graded accordingly to Early Treatment Diabetic Retinopathy (ETDRS) criteria.

Statistical analysis: All data were analyzed using descriptive statistics and Chi square test and contingency coefficient analysis was applied.

**RESULTS:** A prospective study was conducted in the Department of Ophthalmology, K. R. Hospital, and Mysore. In this study 100 patients with diabetes mellitus were analyzed. The youngest was 28yrs and the oldest was 80yrs. The mean age of subjects was 54.16 yrs (Table 1).

Out of 100 diabetes mellitus patients, 44 (44%) had normal fundus picture, 34 (34%) patients had mild NPDR, 10 (10%) patients had moderate NPDR, 10 (10%) patients had severe NPDR and 2 (2%) had PDR (Table 2).

Of 100 subjects, 54(54%) were males and 46(46%) were females (Table 3 and 4) But there was no significant association between sex and frequency of dry eye syndrome ( $P = 0.42$ ).

In the present study, 56 (56%) patients had Diabetic retinopathy and 46(46%) had normal fundus picture. Out of the 56, 34 (60.71%) patients had mild NPDR, 10 (17.85%) patients had moderate NPDR, 10(17.85%) patients had severe NPDR and 2 (3.57%) patients had PDR. Out of the 100 patients, 36 (36%) patients had dry eye. 4 (11.11%) patients with normal fundus, 16 (44.44%) patients of mild NPDR, 8 (22.22%) patients of moderate NPDR, 6 (16.67%) patients of severe NPDR and 2 (5.56%) patients of PDR had dry eye (Table 5 and 6). Significant association ( $P = 0.001$ ) between dry eye and diabetes mellitus was seen.

In our study majority of the dry eye patients complained of burning sensation, stringy discharge and redness. On examination posterior blepharitis was seen in 6(16.6%) patients, fluorescein staining revealed punctate epithelial erosions in 7(19.4%) patients, and conjunctival keratinization was present in 2(5.5%) patients with dry eye.

Conjunctival impression cytology showed moderate degree of keratinization in 2 (5.5%) patients with PDR.

**DISCUSSION:** Dry eye is a clinical condition characterized by deficient tear production or excessive tear evaporation. Keratoconjunctivitis sicca (KCS) refers to any eye with some degree of dryness. It is classified as:

1. Aqueous layer deficiency.
2. Evaporative.

The most common ocular symptoms are feelings of dryness, grittiness and burning that characteristically worsen during the day. Stringy discharge, transient blurring of vision, redness and crusting of the lids are also common.

Posterior blepharitis and meibomian gland dysfunction seen with froth in the tear film or along the eyelid margin, may be present. Conjunctiva may show mild keratinization and redness.

The marginal tear meniscus is a crude measure of the volume of aqueous in the tear film. In the normal eye the meniscus is about 1 mm in height, while in dry eye it becomes thin or absent.

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Cornea may show punctate epithelial erosions that stain with fluorescein, filaments consisting of mucus strands lined with epithelium attached at one end to the corneal surface which stain well with rose Bengal. Mucous plaques consisting of semi-transparent, white-to-grey, slightly elevated lesions of various sizes are usually seen in association with corneal filaments.

Complications which are rare but may develop in very severe cases include peripheral superficial corneal neovascularization, epithelial breakdown, melting, perforation and bacterial keratitis.

### **Some of the investigations to confirm and quantify the diagnosis of dry eye are:**

- Tear film break-up time- abnormal in aqueous tear deficiency and meibomian gland disorders.
- For tear production (Schirmer, fluorescein clearance and tear osmolarity).
- For ocular surface disease (Corneal stains and impression cytology).

Dry eye is generally not curable and management is therefore structured around the control of symptoms and prevention of surface damage.

Diabetes and dry eyes appear to have a common association. Keeping blood sugar levels as tightly controlled as possible is the first step in preventing and remedying dry eye syndrome associated with diabetes. Not only does chronically high blood glucose lead to autonomic neuropathy affecting the tear gland, it also affects the quality of tears by increasing the amount of glucose in those tears and disrupting their normal chemical composition, a factor that also contributes to symptoms of dry eye.

In our study, we analyzed 100 patients with type 2 diabetes mellitus. Out of the 100 patients, 36 (36%) patients had dry eye. 4(11.11%) patients with normal fundus, 16(44.44%) patients of mild NPDR, 8(22.22%) patients of moderate NPDR, 6(16.67%) patients of severe NPDR and 2(5.56%) patients of PDR had dry eye. Significant association ( $P = 0.001$ ) between dry eye and type 2 diabetes mellitus was seen.

All the results in our study are comparable to other studies.

In a study by Masoud Reza Manaviat, Maryam Rashidi et al, the prevalence of dry eye syndrome was 54.3%. Of 199 subjects they examined, 108 patients (54.3%) suffered from dry eye syndrome. There was significant association between dry eye syndrome and duration of diabetes ( $P = 0.01$ ).

Dry eye syndrome was more frequent in diabetic patients with DR ( $P = 0.02$ ). DR was found in 140 patients (70.35%), which included 34 patients (17.1%) with mild non-proliferative DR (NPDR), 34 patients (17.1%) with moderate NPDR, 22 patients (11.1%) with severe NPDR and 25 patients (25.1%) with proliferative DR (PDR). There were significant relation between age, sex and duration of diabetes and DR.<sup>6</sup>

In a study by Kaiserman I et al, significantly higher percentage of diabetic patients (20.6%) received ocular lubrication, compared with nondiabetic patients (13.8%,  $P < .001$ ). The difference was significant for all age groups and for both sexes ( $P < .001$ ). A similar significant difference was prominent between diabetic and nondiabetic patients aged 60 to 89 years who were frequent users of ocular lubrication. Ocular lubrication consumption increased with poorer glycemic control (mean annual HbA1c levels).<sup>7</sup>

In a study by Najafi L, Malek M et al, the prevalence of dry eye disease was 27.7%. A significant correlation between dry eye disease and diabetic retinopathy ( $P=0.01$ ), was found. Dry eye

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disease was more prevalent in people with proliferative diabetic retinopathy and/or clinically significant macular edema (0.006). There was a significant correlation between dry eye disease and retinopathy (OR=2.29, CI=1.16-4.52, P=0.016). In addition, both dry eye and retinopathy had significant correlation with HbA1C.<sup>8</sup>

In a study by Seifart U, Stempel I, 92 patients with diabetes types I and II and aged from 7 to 69 years were compared with a group of normal healthy controls comparable in number, age and sex. The results show that 52.8% of all diabetic subjects complained of dry eye symptoms, as against 9.3% of the controls. A BUT value lower than 10 s was found in 94.2% of the diabetics and in only 5.8% of the controls. Basal secretion test lower than 5 mm was observed in 26% of the diabetics and in 16% of the normal controls. Pathologic conjunctival epithelium (grade III-V after Tseng) was found in 86% of the diabetic patients and in 6.7% of the healthy subjects. Among the type II diabetic patients, 70% had proven dry eye syndrome, while 57% with type I diabetes suffered from this. A correlation was found between the HBA1c values and the presence of dry eye syndrome. The higher the HBA1c values, the higher the rate of dry eye syndrome. The study thus supports the impression that diabetic patients have an elevated incidence of dry eye syndrome. They concluded that close monitoring of diabetic patients and good blood sugar regulation is important for the prevention of dry eye syndrome and retinopathy.<sup>9</sup>

**CONCLUSION:** Dry eye and diabetes mellitus have a common association. Dry eye is more frequent in diabetes mellitus patients with longer duration and in patients with Diabetic retinopathy. Further studies need to be undertaken to establish any etiologic relationship. However examination for dry eye should be an integral part of assessment of diabetic eye disease.

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	Frequency	Percentage
< 30	2	2
31 - 40	6	6
41- 50	18	18
51- 60	36	36
61- 70	28	28
71 - 80	10	10
<b>Total</b>	<b>100</b>	<b>100</b>

**TABLE 1: AGE DISTRIBUTION**

Age(in years)	Normal	Mild NPDR	Moderate NPDR	Severe NPDR	PDR	Total
< 30	2					2
31 - 40	2	2			2	6
41- 50	14	4				18
51- 60	18	6	6	6		36
61- 70	8	16	2	2		28
71 - 80		6	2	2		10
<b>Total</b>	<b>44</b>	<b>34</b>	<b>10</b>	<b>10</b>	<b>2</b>	<b>100</b>

**TABLE 2: GRADING OF DIABETIC RETINOPATHY AND AGE**

	Frequency	Percentage
Males	54	54
Females	46	46
<b>Total</b>	<b>100</b>	<b>100</b>

**TABLE 3: SEX DISTRIBUTION**

	Normal	Mild NPDR	Moderate NPDR	Severe NPDR	PDR	Total
Males	20	20	6	6	2	54
Females	24	14	4	4		46
<b>Total</b>	<b>44</b>	<b>34</b>	<b>10</b>	<b>10</b>	<b>2</b>	<b>100</b>

**TABLE 4: GRADING OF DIABETIC RETINOPATHY AND SEX**

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	<5mm	5-10mm	>10mm	Total
Normal fundus		4	40	44
Mild NPDR		16	18	34
Moderate NPDR	2	6	2	10
Severe NPDR	2	4	4	10
PDR	2			2
<b>Total</b>	<b>6</b>	<b>30</b>	<b>64</b>	<b>100</b>

**TABLE 5: EVALUATION OF DRY EYE IN DIABETES MELLITUS BY SCHIRMER'S TEST**

	<10sec	>10sec	Total
Normal	4	40	44
Mild NPDR	16	18	34
Moderate NPDR	8	2	10
Severe NPDR	6	4	10
PDR	2	0	2
<b>Total</b>	<b>36</b>	<b>64</b>	<b>100</b>

**TABLE 6: EVALUATION OF DRY EYE IN DIABETES MELLITUS BY TEAR FILM BREAK-UP TIME**

### AUTHORS:

1. Tanushree V.
2. H. T. Venkate Gowda

### PARTICULARS OF CONTRIBUTORS:

1. Senior Resident, Department of Ophthalmology, Mysore Medical College & Research Institute, Mysore.
2. Professor & HOD, Department of Ophthalmology, Mysore Medical College & Research Institute, Mysore.

### NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. H. T. Venkate Gowda,  
# 1128, 1<sup>st</sup> Cross,  
Paduvana Road,  
T. K. Layout, Kuvempu Nagar,  
Mysore-570023.  
Email: drvgmmc@gmail.com

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