



Original Research Article

A Prospective Study of Dry Eye Syndrome among Patients with Type 2 Diabetes Mellitus

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Abstract: Introduction: Diabetes is one of the leading health related catastrophes the world has ever witnessed. It affects millions of people all over the world. The reduced corneal sensitivity favors the occurrence of dry eye syndrome (DES) by reducing the blink rate, by decreasing the reflex-induced lacrimal secretion and increasing evaporative tear loss. It affects millions of people all over the world.

Objective: Assessment of incidence of dry eyes in type 2 diabetic patients. **Methods:** A prospective study was carried out to assess the presence of dry eyes and to investigate the relationship of retinopathy with dry eyes. After applying inclusion and exclusion criteria 50 diabetic patients who attended the out-patient department of the Department of Ophthalmology, Ad-din Akij Medical College, Khulna, Bangladesh from July to December 2023. After applying inclusion and exclusion criteria 50 diabetic patients who attended the out-patient department of the Department of Ophthalmology, were selected. **Results:** Out of 50 Diabetic patients, 29 had dry eyes. Mild form of dry eyes was most common (20%). Majority of the patients were between the ages of 40-60 years. There was no significant association of age, sex and duration of diabetes with incidence of dry eyes. Mild form of dry eyes was most common (20%). There was no significant association of age, sex and duration of diabetes with incidence of dry eyes. Abnormal tear break up time was abnormal in 32%. Abnormal Fluorescein staining was seen in 20% study subjects. Moderate non-proliferative diabetic retinopathy was significantly more common in diabetic patients with dry eyes. **Conclusion:** Examination of dry eyes should be an integral part of the assessment of diabetic eye disease so as to improve the patients comfort and to prevent or minimize further structural damage to the ocular surface.

Keywords: Dry Eyes, Type 2 Diabetes, Retinopathy.

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INTRODUCTION

Diabetes is one of the leading health related catastrophes the world has ever witnessed. [1] It affects millions of people all over the world. It estimates that there will be 370 million people with diabetes on the planet by 2030, which is nearly twice the figure reported in 2000. [2] The reduced corneal sensitivity favors the occurrence of dry eye

syndrome (DES) by reducing the blink rate, by decreasing the reflex-induced lacrimal secretion and increasing evaporative tear loss. 2There are numerous DM-related microvascular and macrovascular comorbidities, including ocular complications. The occurrence of retinopathy, papillopathy, cataract, glaucoma, and ocular surface disease in patients with DM were well-investigated

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in previous studies [3–5]. Given its major impact on vision, retinal disease, cataract, and glaucoma have been the major concerns of ophthalmologists [6, 7], whereas minor ocular surface diseases, such as dry eye disease (DED), were often overlooked, with a previous study showing that 51.3% of DM-related dry eye syndrome cases were underdiagnosed [8]. Many theories explain the connection between dry eye and diabetes. Hyperglycemia and microvascular damage to the corneal nerves can block the feedback mechanism which controls secretion of tears. When the ocular surface innervation is disrupted; tears are not secreted properly by the lacrimal gland. Hyperglycemia triggers inflammatory alterations, thus reducing tear secretion. Inflammation is not only a cause, but also a consequence of dry eye. Inflammation results in aqueous deficient dry eye or lacrimal insufficiency. The various complications include recurrent erosions, persistent epithelial defect, punctate keratopathy, increased risk of microbial keratitis, delayed wound healing, neurotrophic keratopathy and corneal scarring leading to permanent vision impairment. The ocular complications among diabetics include cataract, glaucoma and retinopathy. Recently, dry eye has been reported. Early diagnosis and treatment reduces the complications. However, one of the most common, but often neglected complication associated with diabetes is dry eye. Few numbers of studies have been done regarding the tear film abnormalities in diabetics and decrease in tear production has been reported, but the overall data is not conclusive. Moreover, the ocular surface examination is usually ignored in diabetics and much importance is given to Diabetic retinopathy in routine practice. Hence the present study was undertaken to evaluate the amount of tear production, the stability of the tear film and the condition of the ocular surface in diabetic individuals in order to detect possible tear film abnormalities and its association with diabetic retinopathy. This would improve the patient's comfort and prevent or minimize further structural damage to the ocular surface.

METHODS

A prospective study was carried out to assess the presence of dry eyes and to investigate the relationship of retinopathy with dry eyes. After applying inclusion and exclusion criteria 50 diabetic patients who attended the out-patient department of the Department of Ophthalmology, Ad-din Akij Medical College, Khulna, Bangladesh from July to December 2023. All type 2 diabetes mellitus patients above the age of 45 years, including new and review cases were included in the study. Cases excluded were patients with type 1 diabetes mellitus and other unspecified cases, Contact lens users, patients

who have undergone Pterygium excision, Cataract surgery, Keratoplasty, Glaucoma surgeries, patients who have undergone LASIK surgery, on medications such as antiglaucoma medications, antihistamines, tricyclic antidepressants, oral contraceptives and diuretics, patients with features clinically suggestive of Sjogren's syndrome, Rheumatoid arthritis, Parkinson, Lupus, Hypothyroidism, patients on haemodialysis, with chronic lid abnormalities like blepharitis, meibomitis, lagophthalmos, ectropion, trichiasis, blistering mucocutaneous disorders, ocular chemical injuries in the past.

Inclusion criteria

- I. All patients of either sex, in all age groups, diagnosed to have Diabetes Mellitus Type 2 of any duration.

Exclusion criteria

- I. Patients with systemic diseases and local ocular disease/surface abnormalities as assessed by history and clinical examination, other than diabetes mellitus, which are known to cause dry eyes/ocular surface abnormalities.
- II. Patients who were chronic contact lens wearer.
- III. Patients who have had undergone ocular surgeries in the past.
- IV. Patients on local or systemic medications, which are known to cause dry eyes/ocular surface disorders.

After taking informed consent, detailed history regarding patients name, age, sex, occupation, address, presenting symptoms, duration, progression, and associated conditions were recorded. Detailed history regarding diabetes such as type of diabetes, duration, type of treatment, overall control in the past three months (based on sugar levels, HbA1c values if available), FBS and PPBS levels were recorded. Informed written consent was taken from all the patients. A detailed history regarding age, sex, ocular symptoms, and duration of type 2 diabetes mellitus and presence of other diseases was obtained. Detailed ocular and systemic examination was done. All type 2 diabetes mellitus patients were analyzed for dry eye status and presence of diabetic retinopathy changes. Dry eye status was confirmed by TBUT, Schirmer's 1 test and ocular surface dye staining pattern with fluorescein and issamine green strips. Diagnosis is established by positivity of one or more of the tests in one eye and / or both eyes. The worse eye grading of any of the above test mentioned was considered for statistical purposes when different grading was seen in each eye in an individual. The collected data was numerically coded and entered in Microsoft

Excel 2010 and then transferred to SPSS version 23.0. Added data was analyzed with appropriate test. The comparison of Quantitative variables between and within the groups was done using student's t- test, while the Qualitative data was compared using chi-square test. The confidence limit for significance was fixed at 95% level with p-value <0.05.

RESULTS

Table 1 describes that in this study out of 50 Diabetic patients, 29 had dry eyes. Mild form of dry eyes was most common (20%). Table 2 reveals the association of age, sex and duration of diabetes with incidence of dry eye. Majority of the patients were between the ages of 40-60 years. There was no significant association of age, sex and duration of diabetes with incidence of dry eyes.

Table 1: Incidence of dry eye (n=50)

Dry eyes status	No.	(%)
No dry eyes	29	58.0
Mild dry eyes	10	20.0
Moderate dry eyes	8	16.0
Severe dry eyes	3	6.0

Table 2: Association of incidence of dry eyes with age, sex and duration of diabetes (n-50)

		Count	Dry eyes	P-value	OR (Dry eyes)
Sex	Male	24	11	0.733	1.15
	Female	26	11	0.733	1.15
Age in years	<-20	0	0		
	21-30	1	0	0.392	-
	31-40	6	4	0.065	0.580
	41-50	14	6	0.914	0.972
	51-60	16	6	0.479	1.1208
	61-70	11	4	0.683	1.130
	71-80	4	2	0.962	0.978
	>80	1	0	0.392	-
Duration of Diabetes	< 6 months	7	3	0.514	1.106
	6-12 months	3	1	0.498	0.83
	1-5 years	19	8	0.498	0.909
	5-10 years	10	5	0.216	0.751
	10-20 years	11	4	0.258	1.329
	>20 years	2	1	0.561	0.833

Table 3 shows that significantly more fasting and postprandial blood sugar in diabetic patients with dry eyes. Meibomitis and reduced corneal sensation were significantly more common among diabetics with dry eyes (Table 4). Symptoms like redness, watering, stickiness, crusting etc. were

significantly more common among diabetic patients with dry eyes (Table 5). Table 6 shows clinical signs of dry eyes in diabetic patients. 28% of the patients had low tear meniscus and conjunctival abnormalities that included dull and hyperemic congested conjunctiva.

Table 3: Mean blood sugar level (n-50)

Glycemic control	No dry eyes	Dry eyes	T-test	P-Value
FBS in mg/dl	83.90 ± 12.294	179.63 ± 57.28	18.524	< 0.05
PPBS in mg/dl	116.15 ± 10.49	247.75 ± 88.39	16.709	< 0.05

Table 4: Other causes for dry eyes (n-50)

Other causes for dry eyes	Count	Dry eyes	P-value	OR (Dry eyes)
Blepharitis (lids)	2	1	0.379	0.619
Meibomitis	3	3	0.007	-
Reduced corneal sensation	15	10	< 0.01	0.449
LASER	5	2	0.893	1.056
Hypertension	16	8	0.498	0.847

Table 5: Symptoms among study subject (n=50)

Symptoms	Count	Dry eyes	P-value	OR (Dry eyes)
Eye feel Dry	3	3	0.003	-
Gritty feeling	7	5	0.033	3.682
Burning Sensation	6	3	0.549	1.44
Stickiness	3	2	0.034	7.703
Watering	6	3	0.806	1.171
Redness	3	3	0.007	-
Crusting	2	2	0.016	-
Eyes getting stuck	3	3	0.007	-

Table 6: Signs among study subjects (n=50)

Signs	No	(%)
Low Tear Meniscus	14	28.0
Abnormal Precorneal tear film	10	20.0
Conjunctival abnormalities	14	28.0
Dull Cornea	12	24.0

Table 7 reveals the results of various tests result. Abnormal tear break up time was abnormal in 32%. Abnormal Fluorescein staining was seen in 20% study subjects. Schirmer’s test with Anesthesia

is a better test in terms of sensitivity, specificity, Positive Predictive Value, Negative Predictive Value and accuracy followed by Fluorescein staining and then Tear break up time (Table 8).

Table 7: Various tests in study subjects (n=50)

Tests	Normal	Abnormal
Tear Break up time	34	16
Schirmer’s Test without Anaesthesia	42	21
Schirmer’s Test with Anaesthesia	46	5
Fluorescein stain	40	10

Table 8: Diagnostic Statistics of various tests (n=50)

Diagnostic Statistics	Schirmer’s test without Anaesthesia	Schirmer’s test with Anaesthesia	Tear break Up time	Fluorescein stain
Sensitivity	32.14	100	100	100
Specificity	6.25	89.23	63.04	74.36
PPV	64.29	83.33	19.05	52.38
NPV	1.72	100	100	100
Accuracy	26.1	93.14	70.5225	81.665
Kappa	0.075	0.053	0.084	0.083

Table 9 describes the association of retinopathy with dry eyes. Moderate non-

proliferative diabetic retinopathy was significantly more common in diabetic patients with dry eyes.

Table 9: Association of retinopathy with dry eyes (n=50)

Retinopathy	Count	Dry eyes	P-value
No retinopathy	30	11	0.61
Mild Non Proliferative Diabetic Retinopathy (NPDR)	7	3	0.754
Moderate Non Proliferative Diabetic Retinopathy	4	3	0.049
Severe Non Proliferative Diabetic Retinopathy	2	1	0.817
Proliferative Diabetic Retinopathy (PDR)	6	4	0.357
Severe Proliferative Diabetic Retinopathy	1	-	0.395

DISCUSSION

The early diagnosis and treatment of dry eye are essential to avoid complications. The current treatment regimens for diabetic and nondiabetic dry

eye patients are essentially the same. To date, there is no unified treatment option for DES. The application of artificial tears, including surfactants and various viscous agents, is predominately used to improve symptoms [9]. Artificial tears temporarily

improve blurred vision and other symptoms. The drugs with anti-inflammatory effects do not comprise the active components such as growth factors which are contained in normal human tears [10, 11]. The most widely used anti-inflammatory drugs are corticosteroids, nonsteroidal anti-inflammatory drugs, cyclosporin A, tacrolimus, autologous blood serum, and several new drugs which are undergoing clinical trials [10, 12]. In our study, out of the 50 patients who participated, 42% were suffering from dry eye syndrome. According to Beaver Dam Eye Study, 19.8% of Type II Diabetes had dry eyes [13]. Seifart and associates demonstrated that diabetic patients had an increased rate of Keratoconjunctivitis sicca, which may be attributed to decreased corneal sensitivity, neuropathy involving innervation of lacrimal glands and loss of goblet cells. Among the type II diabetic patients, 70% had proven dry eye syndrome [14]. In a cohort study on 3722 patients, Moss et al., showed 18.1% of diabetics had dry eyes [13]. Nepp et al., showed 43% of diabetics having dry eyes in his study [15]. Hom and De Land showed that 52.9% of patients with either diabetes or borderline diabetes had self-reported clinically relevant dry eyes [16]. The prevalence of dry eyes has been seen to affect females more than males [17]. Also, women who used hormone replacement therapy (HRT) had a 69% greater risk of developing dry eye syndrome [18]. Moss et al., showed a 16.7% incidence of dry eyes in diabetic women compared to 11.4% in diabetic men [19]. In present study, though not significant, incidence of dry eye was more in males compared to females. One study suggests that it is increased evaporation and subsequent increase in tear film osmolarity with age that is the more important determinant for dry eyes [20]. This further suggests meibomian gland dysfunction as the underlying etiologic factor. In our present study, increase in age is associated with dry eyes with 39% of the population in the age group of 31-70 years having dry eyes. The probability of dry eyes in more than 80 years couldn't be considered due to decrease in number of patients in that age group. According to Scultz et al., autonomic dysfunction may be another cause for prevalence of dry eyes with increase in age [21]. The prevalence of diabetic microvascular complications is higher in patients with longer duration of diabetes [15]. These individuals are at an increased risk of developing dry eye syndrome. Seifart and associates demonstrated that diabetic patients had an increased rate of Keratoconjunctivitis sicca, which may be attributed to decreased corneal sensitivity, neuropathy involving innervation of lacrimal glands and loss of goblet cells [14]. In our present study, no such association was seen, with 36% patients having dry eyes within the duration of 1-5 years. In our

study, elevated FBS and PLBS were found to be associated with dry eyes in the study, indicating the role of hyperglycemia. This could result in high extracellular fluid osmolarity disturbing the tear production. Kaiserman and associates have reported that good blood sugar regulation is important for prevention and control of dry eye syndrome among diabetic patients [22]. In our study, 6 patients of diabetes had meibomitis, out of which all six had dry eyes and three patients had blepharitis, out of which two had dry eyes. The diminished corneal sensitivity in diabetes would play the same pathogenesis as diabetic neuropathy. There is a significant association between dry eyes and reduced corneal sensation. Diabetes mellitus causes accumulation of sorbitol by the action of aldose reductase on excess glucose contributing to the alteration in epithelium and endothelium and thus causing corneal hypoesthesia [23]. Out of which 29 had dry eyes showing significant association. This could be due to associated meibomitis causing increase in tear evaporation. Structural, metabolic and functional abnormalities are found in the conjunctiva and cornea of diabetic patients. These abnormalities may be responsible for clinical corneal manifestation of diabetes. The tear film has also been reported to be unstable [24]. In evaluating the diagnostic tests for dry eyes, Tear Film Break - Up Time test was said to be a very non-specific test for determination of tear film stability. [1] In our study, Schirmer's test without anaesthesia showing the total tear secretion was < 10mm in 16% and Schirmer's test with anaesthesia showing the basal tear secretion was < 5mm in 7%. Reflex tearing was more affected in our study possibly due to decreased corneal and conjunctival sensitivity, which has been demonstrated in diabetics by electronic aesthesiometry [25]. Fluorescein stain assessing ocular surface damage was positive in around 20% of our patients. When these diagnostic tests were statistically analysed, Schirmer's test with anaesthesia was found to be more accurate followed by Fluorescein staining and then tear break up time. Also, Nepp and associates have shown that severity of Kerato conjunctivitis sicca correlates with severity of diabetic retinopathy [15]. However in our study, there was no relevant association of diabetic retinopathy with dry eyes.

CONCLUSION

Considering increased incidence of dry eyes, early ocular examination in Diabetic patients should be done for early detection of the ocular surface disorders. In order to prevent dry eye syndrome, good glycemic control is important. Examination of dry eyes should be an integral part of the assessment of diabetic eye disease so as to improve

the patients comfort and to prevent or minimize further structural damage to the ocular surface.

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