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Original Article

Dry Eye in Diabetes Mellitus Patients and its Relationship with Diabetic Retinopathy

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Abstract

Introduction: Diabetic mellitus is a clinical syndrome characterized by hyperglycemia caused by absolute or relative deficiency of insulin. The term diabetes was 1st coined by Arashes Cappodocia (81-133 AD). Later, the word mellitus was added by Thomas Willis in 1675. Clinical features similar to diabetes mellitus (DM) were described 3000 years ago by the ancient Egyptians. Diabetes is one of the leading causes of blindness in 20-70-year-old person.

Materials and Methods: Descriptive study consisting of 100 diabetic patients who attended Ophthalmology Department. Type I and Type II DM of either sex were screened for dry eye and diabetic retinopathy over a period of 18 months. Detailed ocular and diabetic history recorded and clinical examination with slit-lamp for anterior segment was done. Schirmer's test (SchT), tear breakup time (TBUT), and tear meniscus height (TMH) test were performed, and results noted. The stage of diabetic retinopathy was determined using direct and indirect ophthalmoscopy.

Results: In this study, 100 diabetic patients participated, of which 20 were Type I and 80 were Type II DM. Dry eye prevalence was maximum in patients who were 50 years of age (53.6%) and above. It was more common in females (60.9%) compared to males (39.1%). SchT showed 15% and 82.5% of Type I and Type II diabetics had dry eye. The TBUT was found to be ≤10 s in 65% of Type II DM. 49% of Type II diabetics had thin TMH. Moderate non-proliferative diabetic retinopathy (NPDR) (33%) was significantly more common in diabetic patients with dry eyes. There were no patients with very severe NPDR. A statistically significant ($P \leq 0.001$) association was found between diabetic retinopathy and dry eye.

Conclusion: DM and dry eyes appear to have common association. Statistically significant correlation was found between dry eye and diabetic retinopathy. Hence, examination of dry eye should be integral part of assessment of diabetic disease as early detection will help to prevent further progression

Key words: Diabetes mellitus, Diabetic retinopathy, Dry eye, Schirmer's test, Tear breakup time, Tear meniscus height

INTRODUCTION

Diabetic mellitus is a clinical syndrome characterized by hyperglycemia caused by absolute or relative deficiency of insulin.[1]

The term diabetes was 1$^{\sigma\tau}$ coined by Arashes Cappodocia (81-133AD). Later, the word mellitus was added by Thomas Willis in 1675. Clinical features similar to diabetes mellitus (DM) were described 3000 years ago by the ancient Egyptians.[2]

Diabetes is one of the leading causes of blindness in 20-70-year-old person.

DM is associated with ocular complications such as chronic inflammation of the lid, acute orbital infection ptosis, hordeolosis, cataract, refractory deviation, neovascular glaucoma, diabetic retinopathy, and palsy of oculomotor nerve.[3,4]

Nearly 47-64% of diabetic patients have primary corneal lesions, during their lifetime like epithelial fragility microcystic edema and bleb formation, persistent

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epithelial defect, recurrent corneal erosion, delayed epithelial healing.

Recently, problem involving the ocular surface is dry eye, and many diabetic patients complain of typical dry eye symptoms, such as burning and foreign body sensation.[5]

The mechanism responsible for dry eye in DM is unclear, but autonomic dysfunction may be responsible.[6]

The importance of tears has long been recognized. In the fifth to fourth century B.C, Hippocrates classified ophthalmic condition as dry or humid.[7]

Hormonal support conditions in the complex interaction of the tear film, larimal gland, and ocular surface and this was consider as a cause for deficiency of tear fluid in dry eye in earlier days.[8]

Dry eye is defined as a clinical condition characterized by deficient tear production or excessive tear evaporation resulting in ocular discomfort. It characterized by ocular irritation resulting from an alteration of tear film.[9]

The present study was undertaken to find out the association of dry eye with DM as its early detection would prevent further progression.

MATERIALS AND METHODS

Study Design

A descriptive study consisting of 100 diabetic patients was undertaken to study dry eye in DM patients and its relationship with diabetic retinopathy.

Source of Data

A total of 100 diabetic patients attending KIMS Ophthalmology OPD Type I and Type II DM of either sex were screened for dry eye in DM and diabetic retinopathy over a period of 18 months.

Sample Size

100 (54% prevalence, 10% precision sample size - 99, round off to 100).

Sampling method: Purposive method.

Inclusion Criteria

1. Both male and female patients with DM willing to participate in study
2. All age group diagnosed to have DM
3. Written consent of parents for those <13 years and from patients more than 13 years.

Exclusion Criteria

1. Patients who have undergone ocular surgery in the past
2. Patients who wear contact lens
3. Patients who are on local or systemic medication which are known to cause dry eye
4. Patient with other ocular surface disease and systemic disease which known to cause dry eye other than diabetic mellitus.

Method of Data Collection

Initially, informed consent was taken, and patient data regarding dry eye was collected in terms of age, sex, locality, presenting symptoms, duration, progression, and associated conditions. Furthermore, history of DM, treatment duration and blood reports of random blood sugar, fasting blood sugar, postprandial blood sugar level was recorded.

Examination

All patients presenting with DM were subjected to complete ophthalmologic examination and brief general systemic examination. Ophthalmic examination by assessing the visual acuity with Snellens chart, detailed anterior segment examination with slit-lamp to know the condition of eyelid, meibomian gland, conjunctival surface, and cornea.

Tear film evaluation was done in the following order.

Tear meniscus height (TMH) was recorded as normal or low under slit lamp; precorneal tear film was observed for debris.

Tear Breakup Time (TBUT) Measurement

A dry fluorescein strip is touched to the inferior fornix with patient instructed to look up.

The corneal surface is seen under slip lamp with low magnification using a cobalt blue filtered light. The patient is asked to blink ones and look straight without blinking. The time of appearance first small black spot within blue field (dry spot) from the last blink measures the tear film BUT. <10 s are taken as abnormal.

Schirmers Test (SchT)

Filter paper is placed in the inferior cul-de-sac from outer one-third and inner two-third and the amount of wetting of the paper strip after 5 min was measured. Normal value of Schirmer I test are more than 15 mm. Wetting of 5-10 mm was taken as moderate and <5 mm is severe.

Based on Schirmers I, TBUT, TMH grading of dry eye was done into 3 types mild, moderate, and severe.

Mild dry eye - Patients who have a SchT of <10 mm in 5 min.

TBUT <10 s with TMH thin or absent.

Moderate dry eye - Patients who have a SchT of <5-10 mm in 5 min.

TBUT <10 s with TMH thin or absent.

Severe dry eye -Patients who have a SchT of <5 mm in 5 min.

TBUT <10 s with TMH thin or absent.

Detailed fundus examination done under direct and indirect ophthalmoscopy under mydriasis.

Retinopathy if present is classified as per Early Treatment of Diabetic Retinopathy Study class such as non-proliferative diabetic retinopathy (NPDR), mild, moderate, and severe NPDR, PDR, early PDR, high-risk PDR.

Statistical Method

Descriptive and inferential statistical analysis has been carried out in this study. Results on continuous measurements are presented on mean ± standard deviation D (min-max) and results on categorical measurements are presented in number (%). The significance is assessed at 5% level of significance. The following assumptions on data are made, assumptions: 1. Dependent variables should be normally distributed, 2. Samples drawn from the population should be random, cases of the samples should be independent.

Chi-square/Fisher exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

Significant figures:

+Suggestive significance (P: $0.05 < P < 0.10$)
*Moderately significant (P: $0.01 < P \leq 0.05$)
**Strongly significant (P: $P \leq 0.01$).

Statistical Software

The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0, and R environment ver. 2.11.1 were used for the analysis of the data and Microsoft Word and Excel have been used to generate graphs, tables, etc.

RESULT

Study Design

Descriptive study consisting of 100 diabetic patients.

In this study, 100 diabetic patients participated, of which 20 were Type I and 80 were Type II DM. Dry eye prevalence was maximum in patients who were 50 years of age (53.6%) and Table 1 shows age distribution of patients. Most of the Type 1 diabetic patients were between 0 and 20 years (65%), and most of the Type II patients were between 51 and 60 years (48.8%).

A prevalence of 38% of dry eye was seen in patients having DM for ≥6-10 years.

Type I and type II DM patients were females with 60% and 53.3%, respectively. The majority of patients (87%) had gritty sensation in the eye suggestive of dry eye (Table 3).

It was more common in females (60.9%) compared to males (39.1%) (Table 4). This Table 4 shows females had dry eye more compare to male but it is not significant statistically.

SchT showed 15% and 40% of Type I and Type II diabetics had dry eye (Table 6). Table 6 shows 40% with Type II DM had moderate dry eye and among Type I DM 15% had mild dry eye. The TBUT was found to be ≤10 s in 65% of Type II DM (Table 7). Table 7 shows 65% of Type II diabetes had low TBUT. 49% of Type II diabetics had thin TMH (Table 5). Table 5 shows 49% of diabetes with Type II had thin TMH (49%) and 13% of Type II had absent TMH. Moderate NPDR (33%) was significantly more common in diabetic patients with dry eyes. There were no patients with very severe NPDR. A statistically significant ($P \leq 0.001$) association was found between diabetic retinopathy and dry eye (Table 8). Table 8 shows association of retinopathy with dry eye, significant association was found between retinopathy and dry eye of which 47.8% of dry eye patients with DM had moderate NPDR.

Table 2 shows significant retinopathy changes of moderate NPDR was seen in 33% of Type II diabetics.

Table 1: Age distribution of patients studied

Age in years	Type of DM		Total (%)
	Type I (%)	Type II (%)	
<10	7 (35)	0 (0)	7 (7)
10-20	13 (65)	0 (0)	13 (13)
21-30	0 (0)	0 (0)	0 (0)
31-40	0 (0)	4 (5)	4 (4)
41-50	0 (0)	19 (23.8)	19 (19)
51-60	0 (0)	39 (48.8)	39 (39)
61-70	0 (0)	14 (17.5)	14 (14)
>70	0 (0)	4 (5)	4 (4)
Total	20 (100)	80 (100)	100 (100)

P<0.001**, significant, Fisher exact test

Table 2: Fundus findings of patients studied

Fundus findings	Type of DM		Total (%)
	Type I (%)	Type II (%)	
0-No retinopathy	18 (90)	16 (20)	34 (34)
1-Mild NPDR	2 (10)	12 (15)	14 (14)
2-Moderate NPDR	0 (0)	33 (41.3)	33 (33)
3-Sever NPDR	0 (0)	16 (20)	16 (16)
4-PDR	0 (0)	3 (3.8)	3 (3)
Total	20 (100)	80 (100)	100 (100)

P<0.001**, significant, Fisher exact test. NPDR: Non-proliferative diabetic retinopathy, PDR: Proliferative diabetic retinopathy

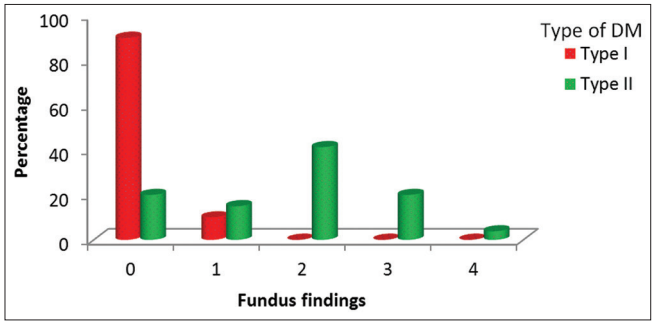
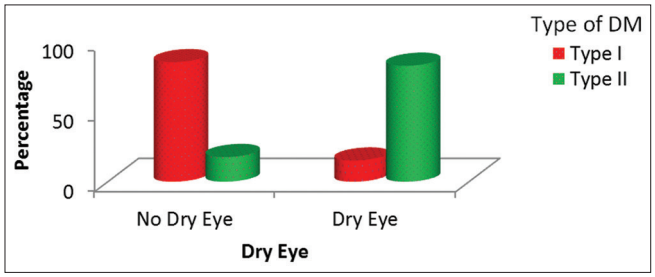


Table 3: Dry eye distribution of patients studied in DM

Dry eye	Type of DM		Total (%)
	Type I (%)	Type II (%)	
No dry eye	17 (85)	14 (17.5)	31 (31)
Dry eye	3 (15)	66 (82.5)	69 (69)
Total	20 (100)	80 (100)	100 (100)

P<0.001**, significant, Chi-square test. DM: Diabetes mellitus



DISCUSSION

There exists a considerable discrepancy between the subjective complaints of patients and the clinical tests available to assess dry eye. It is difficult to correlate test results of TMH, TBUT, SchT in clinical trials.

Each form of dry eye has certain global features which include ocular surface damage, reduced tear hyperosmolarity and tear film stability. Diagnosis of dry eye depends on patients' symptoms, recognition of tear film instability and ocular surface damage. Tear film instability appears to be a component of all forms of dry eye disease, and

Table 4: Gender distribution of patients studied according to incidence of dry eye

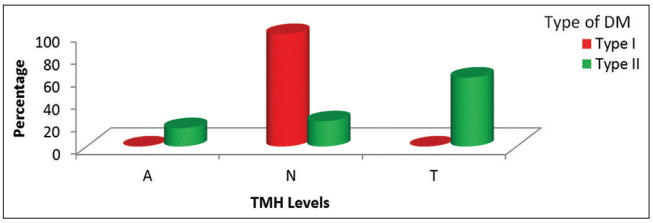
Gender	Dry eye		Total (%)
	No dry eye (%)	Dry eye (%)	
Female	15 (48.4)	42 (60.9)	57 (57)
Male	16 (51.6)	27 (39.1)	43 (43)
Total	31 (100)	69 (100)	100 (100)

P=0.244, Not significant, Chi-square test

Table 5: TMH levels of patients studied

TMH levels	Type of DM		Total (%)
	Type I (%)	Type II (%)	
Absent	0 (0)	13 (16.3)	13 (13)
Normal	20 (100)	18 (22.5)	38 (38)
Thin	0 (0)	49 (61.3)	49 (49)
Total	20 (100)	80 (100)	100 (100)

P<0.001**, significant, Fisher exact test. TMH: Tear meniscus height, DM: Diabetes mellitus



tear hyperosmolarity is a key mechanism of ocular surface damage. Although these elements are present in most cases of dry eye, clinicians will sometimes encounter patients who have symptoms but minimal ocular surface damage or signs of surface damage in the absence of symptoms.

The following types of diagnostic test can identify the global features of dry eye disease,

1. Symptoms questionnaires,
2. Staining to identify ocular surface damage,
3. TBUT to assess tear instability, and
4. Osmometry for tear hyperosmolarity.[10]

In this study, we have made the diagnosis of dry eye based on symptoms, signs and diagnostic tests which included TBUT, TMH and Shirmers test. We observed in our study that a large number of patients had no symptoms or signs of ocular surface damage had abnormal TBUT, TMH, and Schermers test values.

In the present study, the prevalence of dry eyes was found to be 69%. In Type 1 diabetes, it was 15%, and in Type II, it was 82%. Seifart and Strempel,[11] found 57% of dry eye in Type I and 70% in Type II.

Certain aspects of tear physiology change with age, such as tear volume, tear film stability, and reflex secretion by the

Table 6: SchT findings of patient studied

SchT	Type of DM		Total (%)
	Type I (%)	Type II (%)	
0 normal	17 (85)	14 (17.5)	31 (31)
1 mild	3 (15)	15 (18.8)	18 (18)
2 moderate	0 (0)	32 (40)	32 (32)
3 sever	0 (0)	19 (23.8)	19 (19)
Total	20 (100)	80 (100)	100 (100)

P<0.001**, significant, Fisher exact test. SchT: Schirmers test

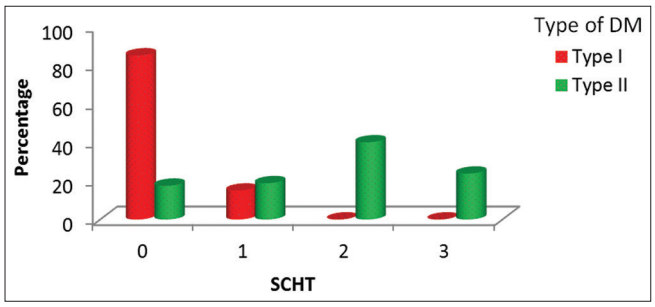


Table 7: TBUT distribution of patients studied

TBUT	Type of DM		Total (%)
	Type I (%)	Type II (%)	
Low	0 (0)	65 (81.3)	65 (65)
Normal	20 (100)	15 (18.8)	35 (35)
Total	20 (100)	80 (100)	100 (100)

P<0.001**, significant, Chi-square test. TBUT: Tear breakup time

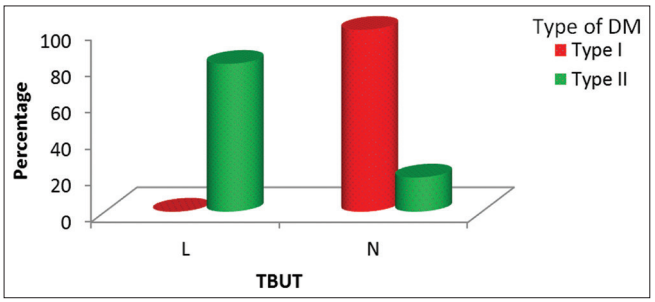


Table 8: Fundus findings according to incidence of dry eye of patients studied

Fundus grading	Dry eye		Total *n*=100 (%)
	No dry eye *n*=31 (%)	Dry eye *n*=69 (%)	
0	26 (83.9)	8 (11.6)	34 (34.0)
1	5 (16.1)	9 (13.1)	14 (14.0)
2	0	33 (47.8)	33 (33.0)
3	0	16 (23.2)	16 (16.0)
4	0	3 (4.3)	3 (3.0)

P<0.001**, significant, Fisher exact test

lacrimal gland. The reflex secretion of tears, as measured by Schirmers I method, decreases significantly with increasing age as already was observed by Schirmer in 1093.[12] The tear evaporation rate has not been found to be correlated with age. It is primarily controlled by the lipid layer of the tear film and lipid layer thickness appears to be constant for different age groups.[13] In the present study, age did not influence the prevalence of dry eyes in Type I patients, but the significant influence was seen in Type II patients after 50 year of age. The majority of Type II DM patients in the age group 0f 51-60 years had dry eyes (53.6%). In the beaver dam eye study, the ageing effect was significant after 65 years of age. Kaiserman *et al.*[14] have reported that the prevalence of dry eye increases with age. Therefore, in the present study, higher prevalence of dry eye in age group 51-60 could be because of DM.

Lee *et al.*,[15] in a population study in Indonesia, showed the prevalence of dry eye was 1.4 times higher for men than women. Moss *et al.*,[16] reported a higher incidence of dry eyes in diabetic women 16.7% compared with 11.4% in men. In the present study, 60.9% of dry eye in diabetic patients were females and 39% were males, but the prevalence of dry eyes was not statistically associated with sex when both Type I and Type II combined. The duration of diabetes was statistically associated with the prevalence of dry eye in DM.

Comparable findings were reported by Seifart and Strempel,[11] Nepp *et al.*,[17] showed that the severity of keratoconjunctivitis sicca (KCS) correlate with the severity of diabetic retinopathy.

Dry eye symptoms tend to be more reliable and accurate than clinical test for dry eye. Often symptoms do not correlate with signs of dry eye.

In the present study, total number of symptoms positive was 69%. Participants complained of gritty sensation most often (87%) followed by symptoms of burning sensation (64%), redness (33%). These symptoms were reported more frequently compared with the other dry eye symptoms and were significantly related with clinical dry eyes.

One of the common objective tests used to make a diagnosis of dry eye is TBUT. Theoretically, TBUT shorter than the blink interval of 5 s could result in surface damage and very short TBUT <2 s indicates KCS.[18]

In the present study, TBUT was found to be ≤10 s in 65%. Tear film breakup time is supposed to be a diagnostic technique in detecting mucin deficient dry eye. Sukul *et al.* found the mean value of TBUT to be 9.67 s in the Indian populations.

A study done by Whitcher[19] found a scanty or absent tear meniscus is an indication of aqueous tear deficiency. In this study, TMH was thin in 49% and absent in 13%.

Lin *et al.*[20] study showed the SchT was shown to be incapable of detecting meibomian gland disease. However, a low Schirmer result (62.5%) was significantly associated with dry eye symptoms in this elderly Chinese population.

The total tears secretion measured by Schirmer I was ≤10 mm in 19%.

Nepp *et al.*[17] were able to correlate the severity of retinopathy with the severity of dry eyes. Kyung-Chulyoon *et al.*, suggest that poor metabolic control, presence of DR stages is risk factors for tear film and ocular surface disorder in DM. In the present study, statistically significant association was found between retinopathy and dry eye ($P \leq 0.001\%$). Therefore, further studies can be undertaken with larger sample size to clarify the association between dry eye and diabetic retinopathy.

CONCLUSION

- Association exists between diabetes and dry eye
- Prevalence of dry eye was more in patients with longer duration of diabetes
- Type I showed mild grade of dry eye and Type II showed mild to moderate grade of dry eye
- In Type II between 50 and 60 years had higher prevalence of dry eye
- Dry eye was more in female patients with diabetes
- Statistically significant correlated was found between dry eye and retinopathy.

Examination of dry eye should be integral part of assessment of diabetic eye disease as early detection will help to prevent further progressions.

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