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Clinical Association Between Dry Eye and Diabetes Mellitus

KEYWORDS: Dry Eye, Diabetes, Mellitus

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ABSTRACT *OBJECTIVE: To study the prevalence of dry eyes and dry eye related ocular surface disorders in diabetic patients.*

SETTING: Tertiary eye care center at asram medical college hospital.

PATIENTS AND METHODS: A cross-sectional clinical study consisting of 150 diabetic patients was undertaken to investigate prevalence of dry eyes.

RESULTS: 150 diabetic patients participated in this study of which 50 (33.3%) were type I diabetes and 100 (66.6%) were type II diabetes. Majority of type I patients were in the age range of 11-20 years (54%), where as majority of type II patients were in the range of 51-60 years (42%). the duration of diabetes in both type I and type II patients. 44% of type I and 37.3% of type II patients had duration of disease ranging between 1-5 yrs. The prevalence of dry eyes in younger age group (≤20) is 2.15 times more compared to older age group in type I diabetics (P=0.468). The prevalence of dry eyes in older age (>50) years group is 2.27 times more in type II diabetics (P=0.095) The crude odds ratio for the association between dry eyes and increasing age (p<0.001, OR 1.02; 95% CI 1.00 to 1.03) was significant.

CONCLUSION: Diabetes and dry eyes appears to be a common association. Predominantly milder grade of dry eye is seen in type I diabetes mellitus and mild to moderate in type 2 diabetes mellitus.

INTRODUCTION:
Diabetes mellitus is associated with a number of ocular complications which can lead even to blindness. Diabetic retinopathy, neovascular glaucoma, cataract, refractory deviations, ptosis, palsy of the oculomotor nerve, and hordeolosis are typical ocular complications in diabeticpatients. Recently, problems involving the ocular surface, dryness in particular, have been reported in diabetic patients. These patients suffer from a variety of corneal complications, including superficial punctate keratopathy, corneal ulceration, and persistent epithelial defects. In addition many diabetic patients complain of typical dry eye symptoms, such as burning and/or foreign body sensation, indicating a clear role for tear film abnormalities.

The present study was undertaken toevaluate the amount of tear production, the stability ofthe tear film and the condition of the ocular surface in diabetic individuals in order to detectpossible tear film anomalies and to evaluate the various risk factors attributable to dry eye. Furthermore, an attempt was made to find any correlation between diabetic retinopathy and dry eyes.

PATIENTS AND METHODS:
This was a hospital based clinical study of 150 diabetic patients who presented to the department of ophthalmology, between July 2012 to june 2014.

All patients of either sex, in all age groups, diagnosed to have diabetes mellitus (by endocrinologists/ as per ADA criteria) of any duration. Exclusion criteria included Patients with systemic diseases and local ocular disease/ surface abnormalities as assessed by history and clinical examination, other than diabetes mellitus,chronic contact lens wearer, undergone ocular surgeries in the past, on local or systemic medications, which are known to cause dry eyes/ocular surface disorders. Ocular examination included recording visual acuity with snellen's chart (in patients with visual acuity less than 6/60, acuity was recorded as counting fingers at particular distance or hand movements or perception of light or projection of rays). Detailed anterior segment examination was done under slit lamp. Condition of lids, meibomian glands, conjunctival surface (dryness, wrinkling, sheen) and corneal surface was noted.

Tear film evaluation was done by TBUT, FLOURESCEIN STAINING SCHIRMMER 1 AND 2 ROSEBENGAL STAIN. The Diagnostic statistics namely, sensitivity, specificity, PPV, NPV, Accuracy and Kappa have been used to find the diagnostic values of the screening tests. The Statistical software namely SPSS 11.0

RESULTS:
Participant characteristics
150 diabetic patients participated in this study of which 50 (33.3%) were type I diabetes and 100 (66.6%) were type II diabetes.

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Table 1: Age distribution

Age in years	Type I		Type II		Total	
	Number (n=50)	%	Number (n=100)	%	Number (n=150)	%
0-10	13	26.0	-		13	8.7
11-20	27	54.0	-		27	18.0
21-30	9	18.0	1	1.0	10	6.7
31-40	1	2.0	9	9.0	10	6.7
41-50	-	-	18	18.0	18	12.0
51-60	-	-	42	42.0	42	28.0
61-70	-	-	24	24.0	24	16.0
>70	-	-	6	6.0	6	4.0
Mean 瀱D	15.20 ± 7.65		55.74 ± 10.59		42.27 ± 21.48	

Table 1 shows the age distribution of the participants. Majority of type I patients were in the age range of 11-20 years (54%), whereas majority of type II patients were in the range of 51-60 years (42%).

Table 2: Sex distribution

Sex	Type I		Type II		Total	
	Number (n=50)	%	Number (n=100)	%	Number (n=150)	%
Female	22	44.0	40	40.0	62	41.3
Male	28	56.0	60	60.0	88	58.7

Table 2 shows the sex distribution in both groups.

Table 3: Duration of diabetes

Duration of diabetes	Type I		Type II		Total	
	Number (n=50)	%	Number (n=100)	%	Number (n=150)	%
≤6 months	5	10.0	9	9.0	14	9.3
6 months-1 years	1	2.0	2	2.0	3	2.0
1-5 years	22	44.0	34	34.0	56	37.3
5-10 years	19	38.0	19	19.0	38	28.3
10-20 years	3	6.0	30	30.0	33	22.0
>20 years	-	-	6	6.0	6	4.0

Table 3 shows the duration of diabetes in both type I and type II patients. 44% of type I and 37.3% of type II patients had duration of disease ranging between 1-5 yrs.

Table 4: Prevalence of Dry Eyes

Dry/No dry Eyes	Type I (n=50)		Type II (n=100)		Total (n=150)	
	No	%	No	%	No	%
No dry eyes	34	64.0	62	62.0	96	64.00
Mild dry eyes	9	18.0	15	15.0	24	16.00
Moderate Dry eyes	6	12.0	18	18.0	24	16.00
Severe Dry eyes	1	2.0	5	5.0	6	4.00

Table 4 shows the pattern of dry eyes in type I and type II diabetes patients. Overall prevalence is 36%. The prevalence was 32% in type I, predominantly mild form (18%) compared with 38% in type II where mild to moderate grade was predominant(32%).

Table 5: Association of age with dry eyes

Age in years (n=150)	Total	Dry eyes	P value	OR (Dry eyes)
0-10	13 (8.7)	3 (2.0)	0.379	0.51
11-20	27 (18.0)	11 (7.3)	0.571	1.27
21-30	10 (6.7)	1 (0.7)	0.076	0.18
31-40	10 (6.7)	4 (2.7)	0.747	1.20
41-50	18 (12.0)	4 (2.7)	0.194	0.47
51-60	42 (28.0)	17 (11.3)	0.476	1.30
61-70	24 (16.0)	9 (6.0)	0.867	1.08
>70	6 (4.0)	5 (3.3)	0.023	9.69

Table 5 shows association dry eyes with the age of patient.

The prevalence of dry eyes in younger age group(?0) is 2.15 times more compared to older age group in type I diabetics (P=0.468). The prevalence of dry eyes in older age (>50) years group is 2.27 times more in type II diabetics (P=0.095) The crude odds ratio for the association between dry eyes and increasing age (p<0.001, OR 1.02; 95% CI 1.00 to 1.03) was significant.

Table 6 : Association of sex with dry eyes

Sex	Total	Dry eyes	P value	OR (Dry eyes)
Male	88 (58.7)	32 (21.3)	P>0.05	1.02
Female	62 (41.3)	22 (14.7)		

Table 6 shows association of sex with dry eyes. The incidence of dry eyes is 2.2 times more for males in type I diabetics (p=0.213) and 1.37 times more for females in Type II diabetics (P=0.449). However the prevalence of dry eyes is not statistically associated with sex when both Type I & Type II were combined.

Table 7 : Association of Duration of diabetes with dry eyes.

Duration of diabetes (n=50)	Total	Dry eyes	P values	OR (Dry eyes)
≤6 months	14 (9.3)	6 (4.0)	0.575	1.38
6 months -1year	3 (2.0)	1 (0.7)	P>0.05	0.88
1-5 years	56 (37.3)	16 (10.7)	0.143	0.59
5-10 years	38 (25.3)	11 (7.3)	0.295	0.65
10-20 years	33 (22.0)	16 (10.7)	0.091	1.95
>20 years	6 (4.0)	4 (2.7)	0.189	3.76

Table 7 shows the association of duration of diabetes with dry eyes. Duration of diabetes is not statistically associated with the prevalence of dry eyes in type I and is significantly associated with the incidence of dry eyes in type II (P=0.022) with OR=2.65 indicating that prevalence of dry eyes is 2.65 times more for >10 years of duration in type II diabetes.

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Table 8: Association of Glycemic control with dry eyes

Glycemic control	No dry eyes (n=96)	Dry Eyes (n=54)	Significance by student t
FBS in mg/dl	138.84±57.78	178.63 ±70.26	Student t=3.700 P<0.001
PPBS in mg/dl	190.58 ± 77.69	252.37±92.51	Student t=4.360 P<0.001

Table 8 compares mean FBS and PPBS levels in dry eyes with no dry eye diabetics. Significantly elevated FBS and PPBS levels are found to be associated with dry eyes (P<0.001)

Table 9 : Risk Factors

Other causes for dry eyes	Type I (n=50)	Type II (n=100)	Total (n=150)
Blepharitis (lids)	7 (14.0)	2 (2.0)	9 (6.0)
Meibomitis	5 (10.0)	11 (11.0)	16 (10.7)
Reduced Corneal Sensation	3 (6.0)	22 (22.0)	25 (16.7)
Laser treatment(PRP)	-	10(10.0)	10 (6.7)
Hypertension	-	24 (24.0)	24 (16.0)

Table 9 shows contributing factors prevalent in this diabetic population. Blepharitis was more prevalent in type I population, meibomitis and reduced corneal sensation more in type II patients

Table 10 : Association of Risk factors with diabetic dry eyes.

Other causes for dry eyes (n=150)	Total	Dry eyes	P value	OR (Dry Eyes)
Blepharitis (lids)	9 (6.0%)	3 (2.0%)	P>0.05	0.88
Meibomitis	16 (10.7%)	12 (8.0%)	P=0.001	6.57
Reduced Corneal sensation	25 (16.7%)	22 (14.7%)	P<0.01	21.31
Laser	10 (6.7%)	4 (2.7%)	P>0.05	1.20
HTN	24 (16.0%)	11 (7.3%)	P=0.274	1.63

Table 11 : Symptoms in type I and type II patients

Symptoms (n=150)	Type I (n=50)	Type II (n=100)	Total (n=150)
Eye feel Dry	1 (2.0)	17 (17.0)	18 (12.0)
Gritty feeling	3 (6.0)	18 (18.0)	21 (14.0)
Burning Sensation	10 (20.0)	31 (31.0)	41 (27.3)
Stickiness	1 (2.0)	7 (7.0)	8 (5.3)
Watering	3 (6.0)	10 (10.0)	13 (8.7)
Redness	2 (4.0)	9 (9.0)	11 (7.3)
Crusting	-	2 (2.0)	2 (1.3)
Eyes getting stuck in morning	1 (2.0)	12 (12.0)	13 (8.7)

Table 11 shows symptoms present in type I and type II patients.

Only 6(12%) patients in type I group were symptomatic, whereas 29(29%) patients in type II were symptomatic. Participants complained of burning sensation most often (27.3% of subjects), followed by symptoms of grittiness (14% of subjects) and dry feeling of eyes (12% of subjects) These symptoms were reported more frequently compared with the other dry eye symptoms and were significantly related with clinical dry eyes.

Table 12 : Association of symptoms with Dry eyes

Symptoms (n=150)	Total	Dry eyes	P value	OR (Dry Eyes)
Eye feel Dry	18 (12.0)	17 (11.3)	P<0.001	43.64
Gritty feeling	21 (14.0)	20 (13.3)	P<0.001	55.88
Burning Sensation	41 (27.3)	37 (24.7)	P<0.001	50.06
Stickiness	8 (5.3)	8 (5.3)	P<0.001	-
Watering	13 (8.7)	11 (7.3)	P<0.001	12.02
Redness	11 (7.3)	7 (4.7)	P>0.05	1.02
Crusting	2 (1.3)	1 (0.7)	P>0.05	1.79
Eyes getting stuck	13 (8.7)	12 (8.0)	P<0.001	27.14

Table 12 highlights the prevalence of symptoms in participants of this study and association of each dry eye symptom with dry eyes. 44 subjects reported at least one of the eight dry eye symptoms often or all the time, of these only 35 had dry eyes. The prevalence of positive symptoms was 29.3%.

Table 13 : Clinical Signs of dry eye.

Signs	Type I (n=50)	Type II (n=100)	Total (n=150)
Low Tear Meniscus	10 (20.0%)	23 (23.0%)	33 (22.0%)
Abn.Precorneal tear film	10 (20.0%)	23 (23.0%)	33 (22.0%)
Conjunctival abnormalities	14 (28.0%)	36 (36.0%)	50 (33.3%)
Dull Cornea	9 (18.0%)	28 (28.0%)	37 (24.7%)
SPK	2 (4.0%)	18 (18.0%)	20 (13.3%1)

Table 13 shows clinical signs of dry eyes in type I and type II patients. Precorneal tear film had either oil droplets or mucous strands or both of these. Precorneal tear film of type I patients had mainly oil droplets in the centre 8 patients (8/16) and/or mucous strands in 8 patients. In type II patients, oil droplets were seen in 13 and mucous strands in 23. Conjunctival abnormalities included dull and dry appearance/conjested in 33.3%. In type I patients 3 had xerosis.

Over all ocular surface damage in type I patients was minimal. Superficial punctate keratopathy was seen in 2 type I patients and 18 type II patients. Filamentary keratopathy was seen in only one type II patient.

Table 14: Shows clinical test results

Tests	Normal	Abnormal	Percentage
Tear Break up time	96	48	32%
Schirmer's with anaesthesia	121	29	19.3%
Fluorescene Stain	120	30	20%
Rose Bengal Stain	113	37	24.6%

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Table 15 : Diagnostic value of clinical tests for dry eyes

Diagnostic-Statistics	Schirmer test I	Schirmer test I with anaesthesia	Tear Breakup time	Fluorescen-eStain	Rose Bengal-Stain
Sensitivity	61.11	53.70	88.89	68.52	83.33
Specificity	97.92	98.96	100.00	100.00	100.00
PPV	94.29	96.67	100.00	100.00	100.00
NPV	81.74	79.17	94.12	84.92	80.00
Accuracy	84.67	82.67	96.00	88.67	90.00
Kappa	0.64	0.58	0.91	0.74	0.80

[PPV-positive predictive value, NPV- negative predictive value]

Table 15 summarizes the sensitivity, specificity, positive predictive value, negative predictive value, accuracy and kappa values of various clinical test used for assessment of dry eyes. Tear break up time is having more diagnostic value in terms Accuracy & kappa followed by Rose Bengal Stain compared to any other screening tests

Table 16 : Retinopathy with type of diabetics

Retinopathy	Type I (n=50)	Type II (n=100)	Total (n=150)
No retinopathy	45 (90.0)	59 (59.0)	104 (69.3)
Mild NPDR	5 (10.0)	13 (13.0)	18 (12.0)
Mod NPDR	0	14 (14.0)	14 (9.3)
Severe NPDR	0	4 (4.0)	4 (2.7)
PDR	0	8 (8.0)	8 (5.3)
Severe PDR	0	1 (1.0)	1 (0.7)

Table 16 shows prevalence of retinopathy in type I and type II patients.

Table 17: Association of Retinopathy with dry eyes

Retinopathy (n=150)	Total	Dry eyes	P value
No retinopathy	105 (70.0)	36 (24.0)	0.504
Mild NPDR	18 (12.0)	7 (4.7)	0.785
Mod NPDR	14 (9.3)	5 (3.3)	0.981
Severe NPDR	4 (2.6)	3 (2.0)	0.133
PDR	8 (5.3)	3 (2.0)	P>0.05
Severe PDR	1 (0.7)	-	P>0.05
Inference	Retinopathy is not statistically associated with the incidence of dry eyes (P>0.05)		

Table 17 shows association of retinopathy with dry eyes. However, no statistically significant association was found between retinopathy and dry eyes (P>0.05%)

DISCUSSION

Dry eye is one of the most common ailment ,accounting patients to visit an eye care professional. With an innumerable increase in patients, presenting with dry eye, resulting from change in lifestyle and environment. With , the revolution in newer diagnostic instrument, and the recent advances in Dry Eyes have aided in its treatment part. However better understanding of the concern and with relevant signs and symptoms,inclusive of external and systemic factors supportive with ideal battery of tests for dry eye will help in early diagnosis of prevailing condition. Every clinician is aware of the considerable discrepancy between the subjective complaints of patients and the clinical tests available to assess dry eye.

Frequently the results of Schirmer's test, Tear Film Break Up Time, Rose Bengal staining and Fluorescein staining do not correlate in clinical trials. An European Community Study , concluded that subjective assessments and objective diagnostic tests have clinical utility as diagnostic tools in tear film disorders. Aqueous tear disease is correlated with ocular surface disease.

Each form of dry eye (tear deficient form or evaporative form) has certain global features in common, including –a set of characteristic symptoms, ocular surface damage, reduced tear film stability, and tear hyperosmolarity. Increasingly, an inflammatory component has become apparent, which contributes not only to symptoms, but also to the disease process itself. For the patient, symptoms are the most important aspect of the disorder, whereas dry eye diagnosis depends additionally on the 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 tear hyperosmolarity is a key mechanism for 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. Tear break up time to assess tear instability, and
4 Osmometry for tear hyperosmolarity.

This study was attributed to the diagnosis of dry eye based on symptoms (questionnaires), signs, surface staining with fluorescein and rose bengal stain, the diagnostic tests which included tear break up time and schirmer's test revealing total and basal secretion . Surprisingly evident studies revealed that patients had no symptoms or signs of ocular surface damage rather abnormal tear break up time or schirmer values. These patients had eventually been enlisted for dry eye diagnosis, as symptoms often do not correlate with signs and signs of ocular surface damage can be a late presentation in the course of dry eyes, resulting unnoticed and clinical miss out of the milder disease entity.

In present study, prevalence of dry eyes was found to be **36%**. In type I diabetes it was 32%(16/50), and type II it was 38%(38/100). In the table given below, prevalence of dry eyes in diabetes reported by various other studies is compared with present stud

Authors	Diabetic	Non Diabetic
Seifart et al.[2]	57% in type I and 70% in type II	-
Moss et al.[4]	18.1%	14.1%
Inoue et al.[5]	22.8%	8.5%
Binder et al.[6]	55% type in I	-
Beaver Dam EyeStudy[7]	19.8% in type II	13.9
Peponis et al.[8]	37%	-
Martin Goebbels[9]	37% in type I	-
Nepp et al.[10]	43%	-
Present study	32% in type I diabetics and 38% in type II	-

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The prevalence of dry eye varies from 18.1% to 70%,thereby showing wide disparity. Much of this disparity stems from the fact that there is no standardisation of the types of patients selected for the study,dry eye questionnaires, objective tests and dry eye diagnostic criteria.

The prevalence of dry is significantly higher in diabetic individuals, affecting 20% to 30%. Seifart et al[46] reported that this was due to loss of conjucntival goblet cells, decreased corneal sensitivity and neuropathy involving the lacrimal gland.

Moss et al[4]reported a higher incidence of dry eyes in diabetic women (16.7% compared with 11.4% in men). In the present study, 21.3% of dry eye patients were males and 14.7% were females. It is 2.2 times more for males in type I diabetics (p=0.213) and 1.37 times more for females in Type II diabetics (P=0.449). However the prevalence of dry eyes was not statistically associated with sex when both Type I & Type II were combined. We might assume that the diabetes-induced KCS has no sex predilection, thus weakening the effect of female sex on KCS. Deficient tear secretion from oestrogen deficiency in menopausal women has been hypothesised to explain sex differences, although studies have found that women on hormone replacement therapy may have an increased risk of dry eye [11].

Women's Health Study[12]

The women's health study (WHS) was a large scale, well-conducted study that consisted of 39,876 female health professionals aged 45-84 who were enrolled in a randomised control trial to assess the effects of aspirin and vitamin E on the prevention of cardiovascular disease and cancer. A four –year follow up questionnaire contained questions relating to the clinical diagnosis of dry eye and symptoms of ocular dryness and irritation.

For the purpose of analysis, those who had a clinical diagnosis of dry eye or experienced ocular dryness and irritation constantly were classified as having dry eye.

In the study , the prevalence of dry eye after four years of follow up was 6.7%. In present study, it consists of 41.33% of female and 58.77 % of male,out of which prevalence in type 1 was more in males in type 1 and in type 2 diabetics, it was more in females.

In another study a group of 140 patients aged 24–93, suffering from dry eye syndrome were assessed. A larger number of dry eye syndrome cases were identified in female patients, especially aged over 50 (80% of female and 20% of male). The most frequent general medical conditions diagnosed in the group of patients were as follows: arterial hypertension (men and women) and diabetes (women)[13].In this present study the incidence of dry eyes is 2.2 times more for males in type 1 diabetics and 1.37 times more for females in type 2 diabetics. However the prevalence of dry eyes is not statistically associated with sex when both type 1 and type 2 were combined.

Janine A , Smith M et al conducted a study in woman with premature ovarian failure and compared them with age matched controls and found that woman with premature ovarian failure were more likely to exhibit ocular surface damage and symptoms of dry eye than age matched controls .This data provided further evidence of multi facted role of sex hormone in the normal ocular surface integrity[13].

Conclusion:

Dry eye are common with association of diabetes.predominantly , milder grade of dry eye was seen in type I and mild to moderate in type II diabetes mellitus.

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