

AN ANALYSIS OF PREVALENCE OF DRY EYE SYNDROME IN TYPE 2 DIABETES MELLITUS PATIENTS

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ABSTRACT

BACKGROUND

Globally, an estimate of 422 million adults are living with diabetes mellitus according to the latest 2016 data from the WHO. In India, as per 2015 data, there were 69.2 million cases of diabetes present. Of these, it remains undiagnosed in more than 30 million people.

Dry Eye Workshop (DEWS) in 2007 improvised the definition for DEWS as follows- "Dry eye is a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance and tear film instability with potential damage to the ocular surface. It is accompanied by occurrence of increased osmolality of tear film and inflammation of the ocular surface."

MATERIALS AND METHODS

In our study, 100 cases of maturity onset of type 2 diabetic patients both male and female between age group 30 and 90 years were studied. All 100 cases of type 2 diabetes patients already on oral antidiabetic drugs, insulin or combined treatment reported to eye OPD directly as well as referred from diabetology and medical OPD and ward were subjected to routine ophthalmological examination including Schirmer's test I, TBUT, corneal sensitivity test, blood sugar fasting and postprandial, blood pressure record, HbA1C in selected cases. Clinical data of all patients, which included sex, age, duration of diabetes, family history of diabetes, BMI as well as a history of other associated hypertension and renal failure were recorded in all patients. HIV association, recent ocular surgery, corneal oedema, viral keratitis, Hansen, post LASIK surgery, meibomian gland dysfunction were excluded from our study.

RESULTS

Sexual prevalence in our study was female with increased prevalence of 60% compared to male of 40%. Age of the patients in the range between 30-40 years 10; 41-50 years 31; 51-60 years 35 and 61-70 years 20 in numbers. In our study, more than 15 years duration of diabetes mellitus 15 cases presented with diabetic retinopathy changes as per ETDRS criteria in the stage of moderate NPDR 11 cases and severe NPDR 2 cases. Mild NPDR changes were present in 11 cases and the duration of diabetes in these individuals between 10-15 years period of type 2 diabetes. With PDR changes, 2 cases were presented with severe dry eye showing less than 5 mm in Schirmer's test 1. The increased prevalence of dry eye in female is multifactorial causes like old age, postmenopausal reduced oestrogen level.

CONCLUSION

In our study, there was 15% of DED cases. All of them were more than 15 years duration of diabetes with moderate-to-severe NPDR and PDR with impaired corneal sensation and reduced TBUT values with age group 51-70 years as increased prevalence. Early detection of dry eye in these diabetic mellitus patient will prevent the corneal complications and visual blindness.

KEYWORDS

Diabetes Mellitus, DED (Dry Eye Disease), Schirmer's Test, Corneal Sensitivity, Dry Eye, Diabetic Retinopathy, NPDR, PDR.

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BACKGROUND

The dry eye disease in diabetes mellitus is 15-33%. Globally, an estimate of 422 million adults are living with diabetes mellitus in 2014 compared to 108 million in 1980 according to the latest 2016 data from the WHO.¹

5% of people with diabetes have type 1 diabetes and type 2 diabetes accounts for 95% of diabetic cases the later is usually associated with old age, obesity, physical inactivity, family history of type 2 diabetes or a personal previous history of gestational diabetes. 2.6% of global blindness is attributed to diabetes.²

In our study, the dry eye cases detected were 15 in number. The dry eye detected cases have impaired corneal sensitivity and Schirmer's test I less than 10 mm in 5 minutes. Recently problems involving the ocular surface in dry eye in particular have been reported in diabetic patients contributing to variety of complications like superficial punctate keratitis, trophic ulceration and persistent epithelial defect.³

Impairment of corneal sensitivity increases with the duration of diabetes mellitus being in direct correlation with the degree of polyneuropathy.^{4,5} Severe polyneuropathy measured by MNSI score showed decreased corneal sensitivity together with a decreased number of long nerve fibre bundles in the sub-basal nerve plexus as per in-vivo confocal microscopic image. Cornea is affected relatively early in the course of polyneuropathy. In all patients with polyneuropathy, the sub-basal nerve densities were significantly reduced. In no or mild-to-moderate neuropathy, the corneal sensitivity remains normal. Only in severe neuropathy, diabetes with amputated leg, prosthetic eye indicate the affection of nerve density and corneal sensitivity and subsequent complications occurs.⁶

The ophthalmic branch of trigeminal nerve carries sensory fibres for the cornea. Ocular sensation is greatest in the centre cornea except in elderly patients where it is more sensitive in the periphery.

Michigan Neuropathy Screening Instrument (MNSI) was used as an indicator of diabetic neuropathy. According to Feldman et al, the sensitivity of MNSI score as a predictor of diabetic neuropathy is 80% and the specificity 95%. The inverse correlation between MNSI score and the corneal sensitivity.⁷

An increase in corneal thickness occurs in early stages of diabetes, but the epithelial thickness does not change further with increased degree of neuropathy. A reduction in neurotrophic stimuli in severe neuropathy may induce a thin epithelium that may lead to recurrent corneal erosions.⁸ The epithelium was thinner in diabetes with severe neuropathy. Decrease in nerve fibre bundles count precede impairment of corneal sensitivity. Epithelial thickness decreases only in case of severe neuropathy. The epithelial thickness and corneal sensitivity impairment increases with duration of diabetes mellitus being in direct correlation with the degree of polyneuropathy. Patients with severe neuropathy usually associated with reduced corneal sensation. Corneal sensitivity decreases only in cases of duration of type 2 diabetes and is inversely correlated with the degree of neuropathy (MNSI score). Corneal nerves may have a neurotrophic effect on epithelial cells. Decreased corneal sensitivity and improper neural regulator in the diabetic cornea apparently leads to problems in epithelial wound healing and occurrence of recurrent erosions.

Diabetic keratopathy has also been thought to represent a form of corneal neuropathy. As the diabetic patients have decreased corneal sensitivity, they are more vulnerable to corneal trauma. The increase in corneal thickness in patients with diabetes in addition to polymorphism in epithelium and endothelium were observed by confocal microscopy.

The reduced basal tear production lending to theory of peripheral neuropathy affecting lacrimal gland function in diabetes of longstanding with complications.⁹ Patients with dry eyes exhibits hypoesthesia after mechanical, thermal and chemical stimulation that appears to be related to damage to the corneal sensory innervation.¹⁰

Eyes with normal fundus have normal corneal sensitivity in diabetes mellitus² those with mild NPDR have normal corneal sensitivity, whereas with moderate-to-severe NPDR decreased corneal sensitivity was noted. Those with PDR and advanced diabetic eye disease showed a greater loss of corneal sensitivity. In pan-retinal photocoagulation received eyes demonstrated most severe reduction in corneal sensitivity. In untreated, diabetic patient corneal hypoesthesia is a form of diabetic sensory neuropathy, while the hypoesthesia associated with laser treatment is attributed to laser damage to sensory nerves lying beneath the choroid. In other words, corneal sensitivity testing can be used as a simple, sensitive and accurate screening tests for proliferative diabetic retinopathy.

Schirmer's test I- <10 mm in 5 minutes is considered abnormal. Tear breakup time >10 seconds is considered normal and less than 10 seconds is considered as tear film instability. Values less than 5 seconds implies severe dry eye.

AIM AND OBJECTIVE

The aim of this study was to analyse the prevalence and various factors contributing to dry eye in 100 cases of only type 2 diabetic individuals. All the patients were studied with reference to sex, age, presence of family history of diabetes, duration of diabetes, type of anti-diabetic therapy, BMI, fundus diabetic retinopathy changes, associated factors like hypertension, chronic kidney disease, TBUT and Schirmer's test I values and the prevalence of dry eye syndrome was studied in these type 2 diabetic individuals.

MATERIALS AND METHODS

Our study is a prospective clinical observational study. The study was conducted in Government Kilpauk Medical College and Hospital, Kilpauk, for a period of one and half months from 1/12/2016 to 17/1/2017. A written consent was obtained from the patients before subjecting them for detailed clinical examination.

100 cases of only type 2 diabetes mellitus patients who reported to eye OPD through referral from diabetology OPD and ward, medicine OPD and ward for routine diabetes eye screening were examined. These patients were already on oral antidiabetic drugs, insulin or both combined therapy. The type 2 diabetic patients associated with contact lens wear, long-standing tricyclic antidepressants, beta blockers, antihistaminics and other associated diseases like rheumatoid arthritis, recent intraocular surgeries, post LASIK surgery, Steven-Johnson syndrome, ocular pemphigoid, pemphigus, lupus, corneal oedema, viral keratitis, Hansen were excluded from our study. Data of all the patients including age, sex, BMI, duration of diabetes, drug history like whether on oral antidiabetic drugs, insulin or both drugs, history of other associated conditions like hypertension,

chronic kidney disease, hyperlipidaemia were obtained by reviewing the medical records and direct patient interview.

The eye complaint like ocular discomfort, gritty sensation, itching, redness, blurring of vision, which improves with blinking, burning sensation were recorded apart from defective vision. Visual acuity examination by Snellen chart distance and near vision examination, cycloplegic refraction, slit lamp examination, intraocular pressure assessment by applanation tonometer, fundus examination by direct and indirect ophthalmoscope, angle of anterior chamber assessment by Goldmann three mirror gonioscopy, tear breakup time, Schirmer's test I, corneal sensitivity test, blood investigation like fasting and postprandial blood sugar, Hb1AC, blood urea and serum creatinine and blood pressure recording were done in all the individuals.

Inclusion Criteria

In our study, both male and female of age group between 35 to 85 years were included. All individuals were only under type 2 diabetes mellitus.

Exclusion Criteria

Other causes of dry eye syndrome like rheumatoid arthritis, HIV positive individuals, recent ocular surgeries, lupus, Parkinson disease, ocular cicatricial pemphigoid, Steven-Johnson syndrome, keratoconjunctivitis sicca, drugs intake like antipsychiatric drug, beta-blockers, diuretics, antihistaminics, tricyclic antidepressant, post LASIK surgery, meibomian gland dysfunction, pregnancy, vitamin A deficiency, corneal oedema, contact lens wearers, viral keratitis, Hansen, glaucoma individuals were excluded from our study. Type 1 diabetes mellitus cases were also excluded from our study.

RESULTS

Male	Female
40	60

Table 1. Sex Distribution of 100 Cases of Diabetes in Our Study

Male	Female
6	9

Table 2. Sex Prevalence of DES Out of 100 Cases of Diabetes in Our Study

Age in Years	Number of Cases
31-40	10
41-50	31
51-60	35
61-70	20
71-80	2
81-90	2

Table 3. Age Prevalence of 100 Diabetic Cases

Age in Years	Number of Cases
31-40	0
41-50	0
51-60	6
61-70	6
71-80	3
81-90	0

Table 4. Age Distribution of Dry Eye Cases Out of 100 Diabetic Individuals

In our study, there were 15 cases of dry eye with type 2 diabetes mellitus. Out of 15 cases, 12 cases fall between 51-70 years age group.

	Number of Cases	Presence/Absence of Dry Eyes
Mild NPDR	11	Absent
Moderate NPDR	11	Present
Severe NPDR	2	Present
PDR	2	Present

Table 5. Comparison of Dry Eye Disease with Various Stages of Diabetic Retinopathy in Our Study

Postprandial Blood Sugar (mg %)	Number of Cases Reported	Dry Eye Disease Associated Cases
140-200	74	NIL
>200	26	15

Table 6. Blood Sugar Values and Duration of Diabetes in Comparison with Dry Eye Prevalence in Our Study

As per WHO classification, postprandial blood sugar more than 200 mg%, 26 cases were reported. Out of 26 cases, 15 patients were associated with dry eye.

Factors Influence on Dry Eye Disease in Type 2 Diabetes Mellitus Patients in Our Study-

1. Increased age.
2. Female sex.
3. Positive family history of diabetes mellitus.
4. Duration of diabetes mellitus.
5. Associated diabetic retinopathy changes.
6. Associated disease like hypertension, polyneuropathy, hyperlipidaemia, chronic kidney disease.
7. Impaired corneal sensitivity.
8. Reduced tear secretion as per reduced Schirmer's test values less than 10 mm in 5 minutes.
9. Persistent hyperglycaemic status values more than 200 mg% for duration of diabetes more than 15 years duration with increased HbA1C value.

Number of Cases on Oral Antidiabetic Drugs	Number of Cases on Combined Insulin and Oral Antidiabetic Therapy
85	15

Table 7. Antidiabetic Treatment Prevalence of Cases in Our Study

HbA1c value reflects the diabetic control status in the individuals for the past three months. Value less than 6.0% is considered as normal. From 6.0 to 6.4% indicates impaired glucose tolerance in the individual. More than 6.5% is considered as diabetic status. We reported higher HbA1c value 8-8.4% in four moderate-to-severe dry eye patients.

Duration of Diabetes	Number of Cases	Number of Dry Eyes
Up to 15 years	74	Nil
16-20 years	11	Nil
More than 20 years	15	15

Table 8. Comparison of Duration of Diabetes in Relation with Dry Eye Manifestation in Type 2 Diabetes

This clearly indicates that more than 20 years duration of diabetes usually controlled with combined oral antidiabetic and insulin therapy alone manifest with impaired corneal sensitivity and dry eye.

TBUT in Secs.	Number of Cases
>10	85
8-10	11
<7	4

Table 9. Tear Breakup Time Values in 100 Cases of Diabetes

Normal	Abnormal	
>10 mm	5-10 mm	<5 mm
85 cases	13 cases	2 cases

Table 10. Schirmer's Test I Values in 100 Diabetic Individuals Study



Figure 1. Schirmer's Test I Value <5 mm in 5 Minutes



Figure 2. Schirmer's Test I Performed in Both Eye Value Showing 5 mm in 5 Minutes

Symptomatology in DED as gritty sensation, itchiness, redness, blurred vision improved with blinking, sensitivity to light and excessive tearing were present in all cases of DED associated diabetic patients. Sore dry eye common in diabetes usually associated with blepharitis.

Higher the HbA1c values, higher the rate of dry eye syndrome.

In our study, the positive family history of diabetes was present in 52% of cases, increased BMI above 25 noticed in 40 percentage of cases, association of hypertension in 22% of cases, chronic kidney disease with severe dry eye and PDR changes was noticed in two cases.

The Schirmer test I values less than 10 mm in 5 minutes was present in 15% of cases. All the 15 cases were presented with moderate NPDR 11 cases, severe NPDR 2 cases and proliferative diabetic retinopathy 2 cases. Tear breakup time less than 10 seconds was present in 15 patients. All the 15 patients showed both eyes impaired corneal sensation tested by whips of cotton wool. To present with impaired corneal sensation and reduced tear secretions leading to DED and its complications in diabetic patients, the duration of diabetic status plays the role. Usually, more than 15 years as well as fundus changes in the form of proliferative diabetic retinopathy and advanced diabetic eye disease association will be present in diabetic patients with dry eye and impaired corneal sensitivity.

Severe impairment of Schirmer's test I, the values less than 5 mm in 5 minutes was noticed in two cases with diabetic of more than 20 year's duration and presence of PDR changes. TBUT less than 7 seconds found in two cases of diabetic with severe NPDR and two cases with proliferative diabetic retinopathy. TBUT between 8-10 seconds in 11 cases of diabetic with moderate NPDR. The polyneuropathy can damage many nerves that are found in the cornea. This will reduce blinking rate and the nerve damage will hinder the person ability to make tears and cause tears to evaporate resulting in dry eye.

Liu et al observed that tear secretion was decreased in diabetes. Jin et al showed that patients with type 2 diabetes tend to develop tear film dysfunction as this study suggest

that TBUT should be routine ophthalmologic test in diabetic patients.²

DISCUSSION

Diabetes is one of the most common leading causes of blindness in 20-74 year old person.¹¹ Brewer Dam study stated the prevalence of DES is 13.3%, which correlated with patient age.

Dry eye was in general higher in women (14.7%) than in men (11.7%).¹²

One of the most common reason for dryness is ageing process.¹³ The mechanism responsible for dry eye is unclear, but autonomic dysfunction maybe responsible.⁶ Aldose reductase, the first enzyme of the sorbitol pathway may also be involved.^{14,15} The oral administration of aldose reductase inhibitors has been shown to improve tear dynamic adequately.¹⁶

The reduced corneal sensitivity in diabetic patients is believed to be a symptom of generalised polyneuropathy that occurs in these patients.¹⁶ Corneal complications of diabetes including superficial punctate keratitis, persistent epithelial defects and corneal endothelial damage have been linked to tear secretion abnormality, decreased corneal sensitivity and poor adhesion between epithelial cells and their basement membrane.¹⁷ Reduced corneal sensitivity is related to the severity of their diabetes, patients with this symptoms were reported to exhibit more severe retinopathy and to have a longer disease duration.¹⁸

Reduced corneal sensitivity contributes to dry eye, as described earlier, it also predisposes patients to corneal trauma leads to greater risk of developing trophic corneal ulcers¹⁹ and adversely affects corneal wound healing.²⁰

In our study of 100 cases of diabetic patients of varying age group, we found 15% of cases were suffering from dry eye. This study correlated with female increased prevalence as female: male in ratio of 9:6 (3:2). DED common with increased age prevalence as the age group between 51-80 years. The percentage of diabetic patients of age group 51-80 years is 57%. Among these age group (51-80 years), in our study, 15 cases were suffering from dry eye disease.

All the 15 dry eye cases came under more than 15 years duration of type 2 diabetes. They were shown Schirmer's test I values less than 10 mm with impaired corneal sensation. The fundus changes among these 15 DED cases, 13 cases revealed moderate NPDR, two cases with severe NPDR and two cases with PDR. TBUT in all 15 cases were less than 10 seconds, while less than 5 seconds in two PDR cases were noted. The positive family history of diabetes in 50% of cases in the study was noted.

The increased age group, increased duration of diabetes, polyneuropathy symptoms with severe NPDR, poor endothelial cell count, impaired corneal sensation, increased female sex prevalence were in correlation with DED in type 2 diabetes were seen.

Corneal neuropathy and microvascular complications associated with diabetes could significantly decrease the tear film function and corneal sensitivity. Tear film changes

in diabetic patients after cataract surgery remains largely unexplored.

In our study, all 100 patients were suffering from only maturity onset type 2 diabetes mellitus and on oral antidiabetic treatment initially and later period landed up to both insulin and oral antidiabetic treatment and increased prevalence of patients between 51 and 70 years age group (55% of cases) were present. Up to 15 years duration of diabetes mellitus, patients usually between the age group 30 and 50 years (41% of cases) did not suffer from dry eye disease. Only after 15 years duration of diabetes mellitus, they landed up with nonproliferative diabetic retinopathy mild stage.

Blood sugar level (postprandial) 140-200 mg% and >200 mg% are considered by WHO, impaired glucose tolerance and diabetes mellitus state, respectively. Moderate and severe diabetes patients invariably suffer from diabetic retinopathy changes if diabetic state last for more than 15 years of duration. All these individuals were suffering from moderate-to-severe NPDR. Severe diabetic state with blood sugar more than 200 mg% lasted for more than 20 years duration of diabetes mellitus with polyneuropathy changes, chronic kidney disease with secondary hypertension and superadded hyperlipidaemia invariably result in proliferative diabetic retinopathy changes and advanced diabetic eye disease in the form of vitreous haemorrhage, neovascular glaucoma and tractional retinal detachment. These patients landed up with severe impaired corneal sensitivity, reduced Schirmer's test values less than 5 mm in 5 seconds and TBUT less than 7 seconds and severe dry eye disease.

Cochet-Bonnet esthesiometer, gas esthesiometer, non-contact esthesiometer can be used to assess the corneal sensation intactness. A cotton wick can be used to assess the presence or absence of corneal sensation in routine clinical practice.

Schirmer's test originally described in 1903 remains the most commonly used technique for assessing the tear secretion. Aqueous tear production is measured by the mm wetted during the test period, usually 5 minutes without topical anaesthetic drug.

CONCLUSION

In our study, the number of participants were 100 only and collected data were only once. DED prevalence in our study was 15% in association with type 2 diabetes mellitus patients.

Corneal complications can be prevented by early detection and early treatment by tear substitutes, topical cyclosporine (0.05%, 0.1%), systemic tetracycline, punctal occlusion, room humidifier and patient education depending upon the cases. Apart from the ophthalmologist to take care of cataract, retina and corneal complications due to DES in long-standing type 2 diabetic patients, their other systems management by general physician, nephrologist, cardiologist and diabetologist to be initiated for the benefit of patients.

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