Estimation of Prevalence of Dry Eye, and Ocular Surface Changes, in Patients of Diabetes Mellitus, in Vijaypur District, India

Anand Gurabasappa Gannur¹, Madhu Guranna Patil², Prabhugouda Basangouda Lingadalli³,
Zameer Hassan Golewale⁴

^{1, 2, 3, 4} Department of Ophthalmology, Al Ameen Medical College and Hospital, Vijaypur, Karnataka, India,

ABSTRACT

BACKGROUND

Diabetes mellitus (DM) is associated with a number of ocular complications such as diabetic retinopathy, cataract, refractory deviations, oculomotor nerve palsy etc. Recently, problems involving the ocular surface, dryness in particular, have been reported with dry eye symptoms, indicating a clear role for tear film abnormalities. The objectives of this study were to estimate the prevalence of dry eye and dry eye related ocular surface changes in diabetic patients, and to study the association between diabetic dry eyes and its relation to age, sex, glycemic control, duration of disease and diabetic retinopathy

METHODS

A hospital based clinical study of 100 diabetic patients who presented to the Department of Ophthalmology, Al Ameen Medical College and Hospital, Vijayapur from November 2019 to November 2020 was conducted. Detailed history was recorded. Assessment of anterior segment via slit lamp biomicroscopy was done. The examinations for dry eyes included Schirmer's test, tear break-up time, fluorescein and rose bengal staining and a questionnaire. The retinopathy was examined by ophthalmoscopy and was recorded.

RESULTS

Of the 100 diabetic patients, 2 (2 %) were type I and 98 (98 %) were type II diabetes. The mean age of type I group was 30 ± 0 years and 57.55 ± 27.07 years in type II group. 50 % were males in type I group, and 51.47 % in type II. Fifty nine (59 %) patients had dry eye. The prevalence in type I was 100 % and in type II was 58.16 %. Dry eye prevalence was maximum in those between 51 to 60 years of age (55.77 %). A 2.65 fold increase was found in the odds for dry eye in those with > 5 years of diabetic duration. The association of dry eye among uncontrolled was statistically highly significant with P value less than 0.001. The tear break up time was found to be ≤ 10 sec in 26 % (26/100). Schirmers test was found to be ≤ 10 mm in 27 % (27/100). Stains (Rose Bengal and fluorescein stain) were found to be abnormal in 18 %. Retinopathy was seen in 100 % of type I and 9.18 % of type II group. Statistically highly significant association was found between retinopathy and dry eyes ($P < 0.001$).

CONCLUSIONS

Diabetes and dry eye appears to have common association. Highly significant statistical correlation was found between retinopathy and dry eyes. Examination for dry eyes should be an integral part of the assessment of diabetic eye disease.

KEY WORDS

Diabetes, Dry Eye, Diabetic Retinopathy

Corresponding Author:

Dr. Anand Gurabasappa Gannur,
"Basava chetana" Shanti nagar,
Jayanagar Colony, Gyangbawdi
Road, Vijaypur - 586101,
Karnataka, Bangalore,
E-mail: anandggannur@yahoo.com

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BACKGROUND

World Health Organization (WHO) estimates that there will be 370 million people with diabetes on the planet by 2030, which is nearly twice the figure reported in 2000. WHO has labeled India as "The diabetic capital of the world" as it has the highest number of diabetics in the world.¹ Diabetes mellitus is associated with a number of ocular complications such as diabetic retinopathy, cataract, refractory deviations, palsy of the oculomotor nerve etc. Recently, problems involving the ocular surface, dryness in particular, have been reported in diabetic patients with typical dry eye symptoms, such as burning and/or foreign body sensation, indicating a clear role for tear film abnormalities. Various earlier studies have reported qualitative and quantitative tear film abnormalities in diabetics, but the precise role of these abnormalities in the pathogenesis of dry eyes is not well defined. More often ocular surface examination is ignored and much importance is given to retinopathy.

TFOS DEWS II (Tear Film and Ocular Surface Society, Dry Eye Workshop) defines dry eye disease as the following: "Dry eye is a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles".² Loss of tear film homeostasis can arise from a multitude of factors that encompass eyelid and blink abnormalities, in addition to ocular surface or tear component deficiencies. These changes can induce focal or global tear film instability and tear hyperosmolarity in response to excessive evaporation from the ocular surface, and are regarded as significant entry points that contribute to the pathogenesis and perpetuation of a cycle of events, or "Vicious Circle", in dry eyes. Emerging over the last decade has been mounting evidence of the potential role of neurosensory abnormalities in the understanding and management of dry eyes. While a comprehensive understanding of the exact role that neurosensory abnormalities play within the pathophysiological pathways of dry eyes is yet to be reached, their potential, is deemed worthy of recognition.²

The tear film has a vital role in providing lubrication and protection to the ocular surface, as well as maintaining a smooth, refractive surface for optimal visual performance. Physiologically, homeostasis describes the state of equilibrium in the body with respect to its various functions, and to the chemical composition of the fluids and tissues. When applied to dry eyes, the concept of disrupted tear film homeostasis acknowledges the possibility of many different changes that can occur in the tear film and ocular surface, in response to one or more of the underlying causes of dry eye. Disruption of homeostasis is considered to be the unifying characteristic that describes the fundamental process in the development of dry eyes.²

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 anomalies. Furthermore, an attempt was made to find any association between diabetic retinopathy and dry eyes.

METHODS

A hospital based cross-sectional study of 100 diabetic patients in Department of Ophthalmology, Al Ameen Medical College, Vijayapur, from November 2019 to November 2020.

Sample Size

With anticipated prevalence of dry eye disease, 53 %^(ref) the minimum sample size is 98 patients with 5 % level of significance and 10 % absolute error.

Formula used

$$n = \frac{z^2 p * q}{d^2}$$

Where Z = Z statistic at α level of significance

d² = Absolute error

P = Proportion rate

q = 100

Inclusion Criteria

All patients of either sex, in all age groups, diagnosed to have diabetes mellitus (by physician or endocrinologists) of any duration.

Exclusion Criteria

1. 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.
2. Patients who were chronic contact lens.
3. Patients who have undergone ocular surgeries in the past.
4. Patients on local or systemic medications, which are known to cause dry eyes/ocular surface disorders.

Method of Data Collection

History

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, fasting blood sugar (FBS) and post prandial blood sugar (PPBS) levels] were recorded. Ethical committee clearance obtained.

Questionnaire

A standard questionnaire of ocular symptoms³ relating to dry eye was used which included the following questions

1. Do your eyes ever feel dry?
2. Do you ever feel a gritty or sandy sensation in your eye?
3. Do your eyes ever have a burning sensation?
4. Are your eyes ever red?
5. Do your eyes ever feel sticky?
6. Do your eyes ever feel watery or tearing?
7. Do you notice much crusting on your lashes?

8. Do your eyes ever get stuck shut in the morning?

Presence of a symptom from the dry eye questionnaire was further graded as rarely (at least once in 3 – 4 months), sometimes (once in 2 – 4 weeks), often (at least once a week), or all the time. Presence of one more symptoms often or all the time was taken as positive.

Examination

A brief general and systemic examination was carried. Ocular examination included recording visual acuity with early treatment diabetic retinopathy study (ETDRS) chart. Detailed anterior segment examination was done under slit lamp. Condition of lids, meibomian glands, conjunctival surface and corneal surface was noted.

Meibomian Gland Status was Graded³ as Follows

- Grade 0 - no disease
- Grade 1 - plugging with translucent serous secretion when compressing the lid margin
- Grade 2 - plugging with viscous or waxy white secretion when compressing the lid margin
- Grade 3 - plugging with no secretion when compressing the lid margin.

Cornea was evaluated in detail for its sheen, surface (SPK, mucous plaques, and filamentary keratitis). Corneal sensation was recorded after Schirmers I test with a fine moist cotton wisp and graded as normal, reduced or absent.

Tear Film Evaluation was Done in the Following Order

Tear meniscus height was recorded as normal or low (under slit lamp, thin beam). Precorneal tear film was observed for presence of debris (mucous/oil droplets/debris)

Tear Break-Up Time (TBUT) Measurement

No anesthesia was used. A dry fluorescein strip is touched to the inferior fornix with the patient looking up. The cornea was scanned under low slit lamp magnification using a blue cobalt filtered light. The patient is instructed to blink once or twice and then stare straight ahead without blinking. The time of appearance of the first dry spot formation (small black spots within the blue - green field) from the last blink measures the TBUT. Values < 10 seconds are taken as abnormal.

Fluorescein Staining of Cornea was Graded from 0 - 3³

1. No staining of corneal epithelial surface.
2. Mild staining occupying < 1/3 of corneal epithelial surface.
3. Moderate staining occupying < ½ of corneal epithelial surface.
4. Severe staining of > ½ of the corneal epithelial surface.

Schirmers Test I

It was performed by placing a precut strip of filter paper (whatman no 41, ContaCare Pvt. Ltd., Baroda) in the inferior cul-de-sac; Patient was asked to blink normally, and the amount of wetting of the paper strip after 5 minutes was measured. Wetting of ≤ 10 mm was taken as abnormal.

The basal secretion test was performed following the instillation of topical anesthetic (4 % xylocaine drops) and the placement of a thin strip of filter paper in the inferior cul-de-sac.

Rose Bengal Stain

This was carried out in the end, a moistened strip of rose bengal (ContaCare Pvt. Ltd., Baroda) was applied to the inferior cul-de-sac, under no anesthesia. Van Bijsterveld scoring system was used to grade the staining of cornea and conjunctiva, based on a scale of 0 - 3 in 3 areas: nasal conjunctiva, temporal conjunctiva, and cornea. With this system, the maximum possible score is 9, a score of 3.5 or greater was considered positive for keratoconjunctivitis sicca (KCS).

Detailed Fundus Examination

This was done under direct and indirect ophthalmoscopy and 90 D slit lamp examination and retinopathy if present was classified as NPDR and PDR.

Statistical Analysis

Following tests have been used for statistical analysis - chi-square test, Fischer's exact test, Odds ratio, Student t test. Diagnostic statistics namely, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy and Kappa have been used to find the diagnostic values of the screening tests.

Dry Eye Severity Level	1	2	3	4*
Discomfort, severity & frequency	Mild and/or episodic; occurs under environmental stress	Moderate episodic or chronic, stress or no stress	Severe frequent or constant without stress	Severe and/or disabling and constant
Visual symptoms	None or episodic mild fatigue	Annoying and/or activity - limiting episodic	Annoying, chronic and/or constant, limiting activity	Constant and/or possibly disabling
Conjunctival injection	None to mild	None to mild	+/-	+ / ++
Conjunctival staining	None to mild	Variable	Moderate to marked	Marked
Corneal staining (severity/location)	None to mild	Variable	Marked central	Severe punctate erosions
Corneal /tear signs	None to mild	Mild debris, n meniscus	Filamentary keratitis, mucus clumping, tear debris	Filamentary keratitis, mucus clumping, teardebris,ulceration
Lid/meibomian glands	MGD variably present	MGD variably present	Frequent	Trichiasis, keratinization, symblepharon
TFBUT (sec)	Variable	b 10	b 5	Immediate
Schirmer score (mm/5 min)	Variable	b 10	b 5	b 2

Table1. Grading of Dry Eye⁴

Must have signs AND symptoms. TBUT: fluorescein tear break-up time. MGD: meibomian gland disease
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RESULTS

Of the 100 diabetic patients who participated in this study, 2 (2 %) were type I diabetes and 98 (98 %) were type II diabetes. The mean age of type I group was 30 ± 0 years and 57.55 ± 27.07 years in type II group. The overall mean age was 56.7 ± 25.25 . 50 % were males in type I group, and 51.47 % in type II. Fifty nine (59 %) diabetic patients had dry eye. The prevalence in type I was 100 % and prevalence in type II was 58.16 %. Dry eye prevalence was maximum in those between 51 to 60 years of age (55.77 %). A 2.65 fold increase was found in the odds for dry eye in those with > 5 years of diabetic duration. The association of dry eye among uncontrolled was statistically highly significant with P value less than 0.001. The tear break up time was found to be ≤ 10 seconds in 26 % (26/100). Schirmer's test was found to be ≤ 10 mm in 27 % (27/100), stains (Rose Bengal and fluorescein stain) were found to be abnormal in 18 %. Retinopathy was seen in 100 % of type I patients, 9.18 % had retinopathy in type II group. Statistically highly significant association was found between retinopathy and dry eyes ($P < 0.001$).

Participant Characteristics

100 diabetic patients participated in this study of which 2 (2 %) were type I (IDDM) diabetes and 98 (98 %) (NIDDM) were type II diabetes.

Dry / No dry Eyes	Type I (IDDM)	Type II (NIDDM)	Total
No	%	No	%
No (n = 100)	%	No (n = 100)	%
Grade 1	-	32	32.65
Grade 2	-	23	23.47
Grade 3	2	2	4
No evidence of dry eye	-	41	41.84

Table 1. Prevalence of Dry Eyes

Table 1 shows the pattern of dry eyes in type I and type II diabetes patients. Overall prevalence is 59 %. The prevalence was 100 % in type I, predominantly of grade 3 (100 %). Comparatively prevalence is 58.16 % in type II, where grade 1 was predominant (32 %).

Duration of Diabetes (n = 100)	Total	Dry Eyes	P Value	Result	Or (Dry Eyes)
1 - 5 years	81	43	$P < 0.001$	HS	1.96
5 - 10 years	15	11	$P < 0.001$	HS	1.05
10 - 15 years	3	2	$P < 0.001$	HS	0.61
15 - 20 years	1	1	$P < 0.001$	HS	0.5

Table 2. Association of Duration of Diabetes with Dry Eyes

Table 2 shows the association of duration of diabetes with dry eyes. Duration of diabetes is significantly associated with the prevalence of dry eyes in type I and similarly is significantly associated with the incidence of dry eyes in type II ($P < 0.001$) with OR = 2.65 indicating that prevalence of dry eyes is 2.65 times more for > 5 years of duration in type II diabetes.

Table 3 shows the association of dry eye with controlled, uncontrolled sugar level. Controlled patients are more than the uncontrolled and among controlled group no evidence of dry eye is major group. All the patients having uncontrolled sugar level have dry eyes. The association of dry eye among

uncontrolled is statistically highly significant with P value less than 0.001.

Dry Eye	Controlled	%	Uncontrolled	%	χ^2 - Value	P - Value	Result
Grade 1	30	25.5	2	0.3	40.963	<0.001	HS
Grade 2	13	11.05	10	1.5			
Grade 3	0	0	3	0.45			
No evidence of dry eye	42	35.7	0	0			

Table 3. Association of Dry Eye with Controlled, Uncontrolled Sugar Level

Tests	Normal	Abnormal	Percentage
Tear Break Up time	74	26	26
Schirmers test	73	27	27
Stains	82	18	18

Table 4. Clinical Test Results

Retinopathy	Total (n = 100) (%)	Dry Eyes (%)	P - Value
No retinopathy	89(89)	48(53.9)	>0.5,ns
NPDR	8(8)	8(100)	<0.001,hs
PDR	3(3)	3(100)	<0.001,hs

Table 5. Association of Retinopathy with Dry Eyes

Table 5 shows association of retinopathy with dry eyes. Statistically highly significant association was found between retinopathy and dry eyes ($P < 0.001$).

DISCUSSION

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 hyperosmolality. Every clinician is familiar with 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. A European community study,⁵ 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.

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.

In this study, we have made the diagnosis of dry eye based on latest TFOS DEWS II definition and DEWS grading, which included symptoms (questionnaires), signs, surface staining with fluorescein and rose bengal stain, and diagnostic tests which included tear break up time and Schirmer's test.

In present study, prevalence of dry eyes was found to be 59 %. In type I diabetes it was 100 % (2/2), and type II it was 58.16 % (57/98). In the table given below, prevalence of dry eyes in diabetes reported by various other studies is compared with present study.

The prevalence of dry eyes varies from 18.1 % to 70 %, thereby showing wide disparity. Much of this disparity stems from the fact that there is no standardization of the types of

patients selected for the study, dry eye questionnaires, objective tests and dry eye diagnostic criteria.

Moss et al.⁶ 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 eyes.⁷

Certain aspects of tear physiology and tear chemistry change with age, such as reflex secretion by the lacrimal gland, tear volume, and tear film stability, whereas others remain more or less unchanged, such as basal tear production. The reflex secretion of tears, as measured by Schirmer's I method (without anaesthesia), decreases significantly with increasing age as already was observed by Schirmer⁸ in 1903 and by many others thereafter. The evaporation is primarily controlled by the lipid layer of the tear film and lipid layer thickness appears to be constant for different age groups.⁹

In the present study, age did not influence the prevalence of dry eyes in both type I and type 2 patients. Majority of type II DM patients in the age group of 51 - 60 years had dry eyes (55.77 %). 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 ($P = 0.214$ or 1.02; 95 %, CI - 6.435 to 22.43) was not significant. The higher incidence of dry eyes in this age group could be partly attributed to ageing. However, in the beaver dam eye study, ageing effect was significant after 65 years of age. Therefore, higher prevalence of dry eye in age group 51 - 60 years in the present study could be because of diabetes per se, selection bias could have also contributed to this since higher number of participants (64 %) were in this age range.

Duration of diabetes was statistically associated with the prevalence of dry eyes in both type I and type 2 patients ($P < 0.001$) with OR = 2.65 indicating that incidence of dry eyes is 2.65 times more for > 5 years of diabetes in type II diabetes. Binder et al.¹⁰ reported that dry eye symptoms affected some type 1 diabetic patients only during the hyperglycemic phases. This could result from high extracellular fluid osmolarity disturbing tear production, rather than representing a chronic complication of diabetes. In type II patients, most of the long term complications of diabetes are well known to correlate with duration, dry eyes could also be a part of this.

In present study, uncontrolled sugar level was significantly associated with dry eyes, indicating some role of hyperglycemia. A few previous studies have also correlated glycemic control and KCS. In diabetic patients suffering from KCS, poorer glycemic control (higher mean annual HbA1c levels) led to a higher annual consumption of ocular lubrication, regardless of age.¹¹ Moreover, in a multivariate analysis, glycemic control was an independent factor in

forecasting consumption of ocular lubrication. Comparable findings were reported by Seifart et al.¹² Nepp et al.¹³ showed that the severity of KCS correlated with the severity of diabetic retinopathy, which is well known to correlate with glycemic control.

One of the common objective test used to make diagnosis of dry eye is tear break up time. However, it is a very rough test for the determination of tear film stability. Large inter-individual and intra-individual deviations can be found even when performed in a standardised procedure. Theoretically, TBUTs shorter than the blink interval of 5 seconds could result in surface damage, and very short TBUTs (less than 2 seconds) indicate KCS.¹⁴ In the present study, TBUT was found to be ≤ 10 sec. in 26 % (26/100).

Much disagreement exists as to the validity and usefulness of this test. False negative and false positive results cloud the usefulness of each test. In spite of inconsistent repeatability, this test enjoys widespread use. In present study, the total tear secretion (measured by schirmer I) was ≤ 10 mm in 27 % (27/100). Thus, the present data suggest that the amount of tearing is more affected in diabetics. It is possible that the decreased amount of tearing in diabetics may be the result of a diminished corneal and conjunctival sensitivity, which has been demonstrated in diabetics by electronic aesthesiometry.¹⁵

Most of the present study patients had grade 1 dry eye, ocular surface damage as assessed by stains (fluorescein and rose bengal stains), was only 18 %.

When all the clinical tests results were statistically analysed, Schirmer's test was found to have more diagnostic value in terms of accuracy & kappa followed by stains (fluorescein and rose bengal stains).

In the present study, statistically highly significant association was found between retinopathy and dry eyes ($P < 0.001$). In earlier study by saito et al.¹⁶ decrease in corneal sensation, but not tear secretion, was correlated with the stage of diabetic retinopathy. However, Nepp and associates¹² were able to correlate severity of retinopathy with the severity of dry eyes. Further studies need to be done to clarify association between these two.

CONCLUSIONS

Diabetes and dry eyes appear to have a common association. Predominantly, grade 3 (severe) dry eye was seen in type I diabetics and grade 1(mild) and grade 2 (moderate) in type II diabetes patients. Higher prevalence was observed in those above 50 years of age in type II diabetics. A 2.65 fold increase was found in the Odds for dry eye in those with > 5 years of diabetic duration. Statistically highly significant correlation was found between retinopathy and dry eyes ($P < 0.001$).

Our study indicates that tear film and ocular surface changes in diabetes mellitus include decreased tear stability and secretion. Our results also suggest that poor metabolic control is a risk factor for tear film and ocular surface disorder in diabetes mellitus.

Schirmer's test is found to have more diagnostic value in terms of accuracy & Kappa followed by stains (Fluorescein and

rose bengal stain). Examination for dry eyes should be an integral part of the assessment of diabetic eye disease.

Data sharing statement provided by the authors is available with the full text of this article at jemds.com.

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