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Clinical profile of ocular surface disorder in patient with diabetes mellitus at tertiary care center of Kumaon region Uttarakhand

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Abstract: Background: Diabetes mellitus is a serious public health issue globally, and India is no exception to its growing prevalence in many emerging nations. In the near future, India will emerge as the global capital of diabetes.
Objective: The objective of this study is to investigate ocular surface changes and ocular surface disorders in patients with diabetes mellitus.
Methods: This cross-sectional observational study was conducted among all known cases of diabetes mellitus aged over 40 years, attending the eye outpatient department and diabetic clinic at Dr. Sushila Tiwari Government Hospital, Haldwani, Nainital.
Results: The mean age of diabetic patients was 60.82±10.23 (41-79) years. The majority of cases were female (59.7%), followed by males (40.3%). The rural population (56%) was more affected by ocular surface disorders in patients with type II diabetes mellitus than the urban population (44%). Homemakers (50.2%) were the largest group, followed by outdoor workers (30.8%), office workers (12%), and factory workers (7%). Itching was present in 22.0%, lacrimation in 54.8%, burning in 66.8%, foreign body sensation in 85.6%, and blurring of vision in 53.2%.
Conclusions: This study establishes a causal relationship between ocular surface disorder and diabetes mellitus.

Keywords: Ocular surface disorder, Diabetes mellitus; Tertiary care center.

1. Introduction

Diabetes is a well-known cause of life-threatening or debilitating complications in various organs, including the heart, kidney, brain, and eye [1]. In the eye, diabetic retinopathy, cataract, glaucoma, keratopathy, chronic dry eye, and refractive abnormalities are common diseases associated with diabetes [2].

According to a clinical study, up to 73.6% of type 2 diabetic patients suffer from corneal complications, such as punctate keratopathy, endothelial dystrophy, and recurrent erosions [3]. Diabetic patients often complain of dry eye symptoms, including dryness, burning, redness, pain, ocular irritation, and easily fatigued eyes. The International Dry Eye Workshop in 2017 classified diabetes as a risk factor for aqueous deficient dry eye [4].

The tear film consists of three layers: the outer lipid layer secreted by meibomian glands, the middle aqueous layer secreted by the lacrimal gland, and the inner mucin layer secreted by goblet cells of the conjunctiva. The ocular surface comprises the cornea, conjunctiva, and also includes the lacrimal gland, meibomian gland, lids, and the sensory and motor nerves that connect them [5].

During the course of diabetes, various factors such as hyperglycemia-induced microvascular damage to the lacrimal gland, reduced lacrimal innervation due to autonomic neuropathy, reduced trophic support to the lacrimal tissue, and impaired corneal sensitivity, all contribute to the altered tear film status in diabetic patients [6].

The ocular surface is one of the most complex tissues of the body, and its stability enables protection and effective refractive media for good vision. Hence, any condition that affects the stability and functioning of the tear film can lead to ocular surface disease and dry eye syndrome [7].

According to Dry Eye Workshop (DEWS) II 2017, the definition of dry eye has been revised as a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film. It is accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles [8].

Dry eye (DE) is a multifactorial pathology characterized by a progressive dysfunction of the lacrimal and meibomian glands. It typically leads to decreased aqueous tear production and increased tear evaporation, respectively [9]. These disorders are associated with signs and symptoms of ocular discomfort such as stinging, eye watering or redness, and may cause serious irritation to the interpalpebral ocular surface, particularly the cornea [10].

Although several tests are available for the detection and diagnosis of dry eye, only three tests are routinely used in clinical practice. These are the Schirmer's test, the tear film break-up time (TBUT), and the Rose Bengal test. The latter is reserved for use in severe dry eye patients with corneal signs of dry eye. The Schirmer's test measures the quantity of tear production, and the TBUT measures the quality of the tear. The TBUT is also considered a measurement of the mucin and lipid layer integrity. Hence, this study aimed to investigate the ocular surface changes and ocular surface disorders in patients with diabetes mellitus.

2. Materials and Methods

This cross-sectional observational study was conducted among all known cases of diabetes mellitus aged over 40 years who were attending the eye outpatient department and diabetic clinic of Dr. Sushila Tiwari Government Hospital, Haldwani, Nainital. Informed consent was obtained from patients who participated in the study, and ethical clearance was obtained from the Board of Studies and the institutional ethical committee. The study period was from January 2021 to July 2022.

2.1. Sample size

The study population was determined using G-power software with 80

$n = \frac{Z^2 p(1-p)}{d^2}$

where n is the sample size, Z is the Z-score associated with the desired confidence level (here, 1.96 for a 95% confidence level), p is the prevalence of dry eye in diabetes (18.4%), and d is the absolute error or margin of error, which was set to 5%.

By plugging in these values, the calculated sample size was 231. To account for a non-response rate of 10%, the final sample size was increased to 254.

2.2. Inclusion criteria

Patients attending the outpatient department (OPD) of the eye and diabetic clinic of STH, who are known cases of Diabetes Mellitus and are above the age of 40 years with:

1. Fasting blood glucose levels greater than 126mg/dL
2. Postprandial blood glucose levels greater than 200mg/dL
3. HbA1c levels greater than 6.5%

2.3. Exclusion criteria

1. Individuals with abnormalities in eyelids, cornea, conjunctiva.
2. History of ocular surgery within the past year and active inflammation in the eyes within the last three months.
3. History of ocular chemical injury and chronic ocular drug abuse.
4. Patients who wear contact lenses.
5. Cases of gestational diabetes.
6. Patients with any systemic or autoimmune disorder associated with dry eye.
7. Patients who are not willing to participate.

2.4. Data collection

The patients are asked for the following details:

1. Demographic profile (Name, Age, Gender, Occupation, and Address)
2. Socioeconomic status (according to Modified Kuppuswami scale)

2.5. Study procedure

A detailed history, complete physical examination and routine & appropriate investigations were done for all patients. Patients were asked about the subjective complaints suggestive of OSD including itching, burning, lacrimaion, foreign body sensation etc. If, more than 2 symptoms are present, it is classified as dry eye.

2.6. Ophthalmological examination

BCVA (Best Corrected Visual acuity) with Snellen's chart. Anterior Segment examination by Slit Lamp Examination. Posterior Segment examination with indirect ophthalmoscopy.

2.7. Tear break up time test

An impregnated fluoresce in strip moistened with saline is instilled into the lower fornix. Patient is asked to blink several times. Tear film is examined at the slit lamp with a broad beam of cobalt blue filter. The interval between the last blink and the appearance of the first corneal dry spot in the stained tear film was measured. A TBUT value > 10seconds is normal, 8-10 seconds is mild dryness, 5-7 seconds is moderate dryness, <5 seconds is severe dryness.

Table 1. Tear break up time test grading

Time taken between the last blink and appearance of first corneal dry spot in the stained tear film	**Symptoms**
>10 seconds	Normal
8-10 seconds	Mild dryness
5-7 seconds	Moderate dryness
<5 seconds	Severe dryness

2.8. Schirmer's test

It is useful in the assessment of aqueous layer deficiency. Test involves measurement of amount of wetting of special (No. 41 whatmann) filter paper, 5mm wide and 35 mm long. The test can be performed with or without topical anaesthesia.

In theory, when performed with an anaesthetic (Schirmer II), basic secretion is measured and without anaesthetic (Schirmer I), it measures maximum basic plus reflex secretion. Schirmer folded at the notch and placed at the junction of middle and lateral 1/3 of lower eyelids & allow to stay in place for 5 min, with patients eyes gently closed. Filter paper was removed, the amount of wetting was measured. More than 10mm considered normal, 8-10 mm is mild dryness, 5-7 mm is moderate dryness, <5mm is severe dryness.

Table 2. Schirmer's test grading

Amount of wetting on whatmann no 41	**symptoms**
>10mm	Normal
8-10mm	Mild dryness
5-7mm	Moderate dryness
<5mm	Severe dryness

Figure 1. Schirmer's test

2.9. Rose bengal staining

It is done using saline moistened Rose Bengal strips placed in lower fornix. As described by van Bijsterveld, staining of nasal and temporal conjunctiva is graded from 0-3.

Table 3. Grading of rose bengal staining

Grade	Staining
Grade 0	No staining
Grade 1	Staining of few points
Grade 2	Scattered pattern of staining
Grade 3	Staining of confluent areas of ocular surface

Figure 2. Rose bengal strips

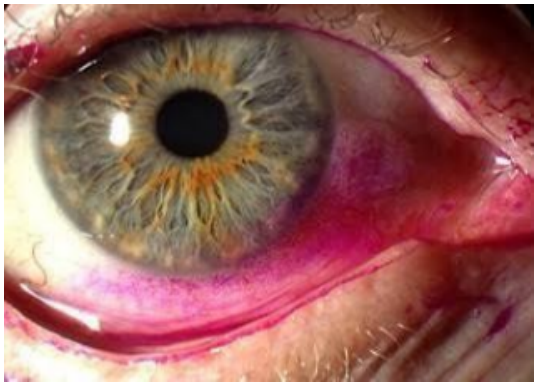

Figure 3. Rose bengal stain

2.10. Rose bengal stain

2.10.1. Statistical analysis

The data was entered into the Microsoft excel and the statistical analysis was performed by statistical software SPSS version 21.0. The Quantitative (Numerical variables) were present in the form of mean and SD and the Qualitative (Categorical variables) were present in the form of frequency and percentage. The p-value was considered to be significant when less than 0.05

3. Results

Total 700 eyes of 350 Diabetic subjects, 210 cases were symptomatic and 140 cases were asymptomatic. However, in symptomatic group, Signs for ocular surface disorder were present in 132 cases and in asymptomatic group, Signs for ocular surface disorder were present in 22 cases. Ocular Surface Disorder was diagnosed in 154 cases (44%) out of 350 patients with Type II Diabetes Mellitus. 196 patient were not having any clinical sign of OSD, hence excluded from study. 154 patients were considered study subjects, see Table 4.

Table 4. Distribution of study subjects according to presence of Symptoms and Signs of Ocular Surface Disorder in Patients with Type II Diabetes Mellitus

Patient category	Asymptomatic	Symptomatic	Total number of patients	Total
Presence of Ocular Surface disorder signs	22 (15.7%)	132 (62.9%)	154	44%
Absence of Ocular Surface Disorder signs	118 (84.3%)	78 (37.1%)	196	56%
Total	140 (40%)	210 (60%)	350	100%

Majority (38.4%) of the subjects belong to age group61-70 years(38.4%) followed by 51-60 years (24.0%), 41-50 years (22.0%) and Above 70 years (15.6%). Youngest patient with Type II Diabetes Mellitus was 40 years of age, while Oldest patient with Type II Diabetes Mellitus was of 85 years. Mean $\pm$ SD age of Diabetic patients had been 60.82$\pm$10.23 (41-79).

Total of 154 patients, 62 (40.3%) were males and 92(59.7%) were females, with M : F ratio of 0.67. Diabetic Females have a slightly higher preponderance of 59.7%, for Ocular Surface Disorder.

Majority (86) of study subjects belong to rural residence (56%) than 68 cases of urban residence (44%).

Majority of study subjects are homemaker 77 patients(50.2%), followed by Outdoor Workers 47 patients (30.8%), Indoor workers 18 (12%) and least common in Factory workers 12 patients (7%), see Table 5.

Table 5. Distribution of study subjects according to Occupation

Occupation	Number of patients	Percentage
Outdoor Workers/ Farmers	47	30.8%
Indoor workers/ Office workers	18	12%
Homemaker	77	50.2%
Factory Workers	12	7%
Total	154	100%

Most of the subjects belong to 58 patients of Upper Lower class (38.0%) followed by 45 patients of Lower Middle (29.2%), 36 patients of Upper class (23.6%), 14 patients of Lower class.

Itching was present among 22.0% cases, Lacrimation among 54.8% cases, Burning among 66.8% cases, Blurring of vision among 53.2% cases and Foreign Body Sensation among 85.6% cases. Most common symptom is Foreign Body sensation (85.6%), see Table 6.

Table 6. Distribution of study subjects according to symptoms, of Ocular surface disease

Symptoms of Ocular Surface Disorder	**Number of patients**	**Percent**
Itching	34	22.0%
Lacrimation	84	54.8%
Burning	102	66.8%
Blurring of vision	82	53.2%
Foreign Body Sensation	131	85.6%

Height of tear menisci was less than 0.2mm in 40.6% patients and 0.2mm-0.5mm in 59.4% patients, see Table 7.

Table 7. Distribution of study population according to Tear Menisci

Tear menisci	**Number of patients**	**Percent**
<0.2	62	40.6%
0.2-0.5	92	59.4%
Total	154	100%

Dry Eye was seen in majority of the patients (49.5%), followed by Pterygium/Pinguecula (15.4%). Conjunctival Hyperaemia in interpalpebral area seen in (14.9%), Posterior Blepharitis seen in 9.2% cases, followed by Anterior Blepharitis in 5.1% cases. Punctitis seen in 3 % cases and Filamentous Keratitis in 2.9% cases.

Cornea sensitivity was decreased among 15.2% subjects, see Table 8.

Table 8. Distribution of Study Population according to the presence of Signs of Ocular Surface Disorder

Signs of OSD	**Number of patients**	**Percentage**
Anterior Blepharitis	09	5.1%
Posterior Blepharitis/ MGD	17	9.2%
Punctitis	05	3.0%
Pterygium/ Pinguecula	10/18	15.4%
Conjunctival Hyperaemia in Interpalpebral Area	27	14.9%
Dry Eye	89	49.5%
Filamentous Keratitis	04	2.9%

Number of patients having diabetic retinopathy with Ocular Surface Disorder is 115(74.8%) , out of which 80(51.8%) patients are having Non proliferative Diabetic Retinopathy and 35(23%) patients belongs to Proliferative Diabetic Retinopathy . Patients not having diabetic retinopathy is 39 (25.2%), see Table 9.

Table 9. Distribution of patients according to Fundus Findings in Diabetes Mellitus patients

Fundus	Number of patients	Percentage
WNL	39	25.2%
NPDR	80	51.8%
PDR	35	23%
Total	154	100%

Majority of cases (114) were having Bilateral involvement (74.2%), and 40 out of 154 cases were having Unilateral involvement (25.8%).

Diabetes was controlled in 99 cases, while it was poorly controlled in 55 cases. Out of controlled group, 84 patients were on Oral Hypoglycaemic agents and 16 patients were on Injection Insulin. Out of Poorly Controlled group, 40 patients were on Oral Hypoglycaemic agents and 15 patients were on Injection Insulin. Diabetes were controlled in majority of the cases (64.2%).

24 patients(15.4%) out of 154 had duration of Diabetes less than5 years, 93 patients(60.3%) had duration of Diabetes between 5-10 years and rest 37(24.3%) had duration of Diabetes more than 10 years of age.

There was a significantly negative correlation of Duration of DM with SCHIRMER I, SCHIRMER II and TBUT.

TBUT was Normal among 77 patients out of 154 cases (50.2%), Mild among 52 cases(33.2%), Moderate among 19 cases(12.2%)and Severe among 6 cases (4.4%).

SCHIRMER I was Abnormal among 43.8%of patients and SCHIRMER II was Abnormal among 52.4% of patients.

4. Discussion

The Present study was aimed to study the profile of Ocular Surface Disorder in patients with Type II Diabetes Mellitus. It incorporates both, the quantitative analysis of symptoms and diagnosis of Ocular Surface Disorder based on symptoms and the clinical tests.

Mean age of Diabetic patients had been 60.82 $\pm$10.23 (41-79) years. This result of our study is concordant with many of the following studies like Badr *et al.,*[11] reported that the mean age was 53.50$\pm$5.37 years in diabetics and 56.48$\pm$4.63 years in the control group. The findings of Yoon *et al.,*[12] demonstrated that there were no statistically significant differences in terms of age between the diabetes and normal control groups.

Diabetic females have a slightly higher preponderance of 59.7%, for Ocular Surface Disorder. As eye is a locus of action of female sexual hormones. Reduction of naturally occurring estrogen is a possible reason for the occurrence of dry eye in post-menopausal women[13]. Caterina Gangliano *et al.,* suggested that deficiency in estrogen sex hormone may lead to reduction in tear production (aqueous deficient dry eye) and meibomian gland dysfunction (evaporative dry eye)[14].

Deficiency of estrogen may lead to reduction in tear production and meibomian gland dysfunction, contributing to the maximum prevalence of OSD in homemakers. Ultraviolet radiation exposure is a common risk factor leading to OSD in outdoor workers.

As majority of the population approaching to eye opd belong to Upper lower class, and awareness of OSD among lower class is poor, therefore they neglect the need for maintaining the quality of life and requiring the treatment of OSD. Patel *et al.,*[15] found that 37% of the subjects had high level of occupation and concluded that DED is associated with work productivity loss and impairment of daily activities.

Foreign body sensation is the most common symptom present in our study population. This result was supported by a study done by Dhwanit Khetwani [16], who studied 182 total subjects with Diabetes Mellitus, and concluded that most common complaints of the subjects were Foreign body sensation followed by itching and watering of eyes.

Dry eye is the most common ocular surface disorder (49.5%), observed in our study. In the similar study done by Khetwani[16], prevalence of dry eye was 45.6%. In a study by Nepp[17] , the Dry eye was seen in 43% of patients.

Manjula *et al.,* [18] concluded that diabetes can cause changes in ocular surface with respect to both qualitative and quantitative parameters. Diabetic patients are more susceptible to dry eye disorders and Meibomian gland disorders when compared to non-diabetic patients.

According to Lee *et al.*,[19] blepharitis has a substantial connection to metabolic disorders like diabetes and may function as an early indicator of this condition. Both Hom *et al.*,[20] and Ansari *et al.*,[21] came to the same conclusions in their respective research. According to the findings of this research, 44% of patients had MGD of Grade 0, 39% had MGD of Grade 1, 9% had MGD of Grade 2, and 8% had MGD of Grade 3, indicating that there is a strong link between the severity of dry eyes and grades of MGD. 56% of the patients in the research had dry eyes, and 24 of those patients had MGD, according to the findings of Manjula *et al.*,[18] The meibomian gland is responsible for the synthesis and production of lipids and proteins, both of which are found in the tear film's outermost layer. These lipids prevent the tear film from drying out and contribute to its overall stability. The results of an international workshop on meibomian gland dysfunction[22] showed that meibomian gland dysfunction (MGD) is the most common cause of evaporative dry eye and may also play a role in aqueous-deficient dry eye.

Cornea sensitivity was decreased among 15.2% subjects. In diabetic patients, corneal sensitivity is reduced due to loss of corneal nerve fibers, which leads to corneal keratopathy.

5. Conclusion

The control of diabetes and its early diagnosis, treatment, and management may enhance quality of life. In order to avoid potential corneal problems, Ocular Surface Disorder patients should begin therapy as soon as possible. The prevention of Ocular Surface Disorder and diabetic retinopathy depends on careful monitoring of diabetic patients and appropriate blood sugar control.

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Conflicts of Interest: "The authors declare that they do not have any competing interests."

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