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Dry Eye and Corneal Sensitivity in Patients with Type 2 Diabetes Mellitus

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Abstract
Background: *Ocular surface disorders in diabetes mellitus have gained significant attention in recent years, as there is increased reporting of the association of dry eye and diminished corneal sensitivity in these patients. However there is a wide variation in the reported prevalence rates, and a detailed ocular surface evaluation is still not routinely performed for all diabetic patients. We decided to undertake this study to study the prevalence of dry eye and corneal sensitivity in patients with and without type 2 diabetes mellitus, and to look for evidence of any association of these two conditions with diabetic retinopathy*
Materials and Methods: *This was a cross sectional study undertaken in patients presenting to the ophthalmology outpatient department. Patients above the age of 40 years who did not have any condition other than type 2 diabetes mellitus that could influence dry eye an corneal sensitivity were taken up for the study. Specific evaluation included a history of symptoms related to dry eye using the 5-Item Dry Eye Questionnaire, and then tear film evaluation, tear film break up time, fluorescein and lissamine green staining and Schirmer I test and corneal sensitivity testing with a Cochet-Bonnet esthesiometer.*
Results: *The prevalence of dry eye among diabetics was 48.9% and diminished corneal sensitivity was 28.9% as compared to 5.6% for both among the non-diabetics. There was a significant association with age and duration of diabetes but not with retinopathy.*
Conclusion: *A detailed ocular surface evaluation is recommended for all patients with diabetes to detect early evidence of ocular surface disorders so that institution of appropriate management may be undertaken at the earliest.*
Keywords: *Dry eye, diabetes, corneal sensitivity, corneal sensation, retinopathy.*

Introduction

Retinopathy, renal disease and generalised neuropathy are the major complications of diabetes mellitus. There is less focus on other manifestations of diabetes like ocular surface disorders, possibly due to a poor understanding of the impact of diabetes on these structures.(1)

The global prevalence of diabetes is projected to reach 366 million by the year 2030.(2) Consequently the morbidity due to ocular surface disease is expected to increase.

According to the Tear Film and Ocular Surface Society (TFOS) Dry Eye Workshop (DEWS) II report, dry eye is a multifactorial ocular surface disease with loss of tear film homeostasis being

the main defining characteristic of the disease.[3] Aging, autonomic dysfunction and involvement of the aldose reductase pathway in diabetes are some of the possible proposed mechanisms for dry eye in patients with diabetes mellitus.[4] Although most studies show an association between dry eye and diabetes mellitus, there is a wide difference in the reported prevalence rates of dry eye, ranging from 18.1 % [5] to 70%. [6]

Various types of corneal dysfunction can occur in diabetes, and can be a cause for significant morbidity in diabetics. Up to 70 % of diabetics suffer some form of corneal dysfunction.[7] The major cause for this is widely accepted to be due to reduced corneal sensation. Since there is a wide variation in the reported prevalence of dry eye disease, we decided to undertake this study to study the prevalence of dry eye and corneal sensitivity in patients with and without type 2 diabetes mellitus, and to look for evidence of any association of these two conditions with diabetic retinopathy.

Materials and Methods

The study was undertaken after obtaining approval from the institutional ethics committee and conformed to the tenets of the declaration of Helsinki. Patients attending the ophthalmology outpatient department and who were eligible were taken up for the study after obtaining written informed consent.

Patients above the age of 40 years and who did not have any exclusion criteria were taken up for the study. Patients who gave a history of, or those that had evidence of systemic or ocular disease, or those who were on local or systemic medication that could influence the state of the ocular surface and corneal sensation were excluded from the study. Type 1 diabetics, contact lens wearers and patients with a history of past ocular surgeries were also excluded. If the patient was not a known diabetic, fasting, post-prandial blood sugars and HbA_1C were performed.

A detailed history and ocular examination was carried out. Symptoms were assessed using the 5-Item Dry Eye Questionnaire (DEQ-5). Detailed ocular surface evaluation included examination of the eyelids, tear film evaluation, tear film break up time, fluorescein and lissamine green staining [8] and Schirmer I test (with and without anesthesia). Corneal sensation was recorded after Schirmers test (without anesthesia) with a Cochet-Bonnet esthesiometer and graded as normal (5-6 mm) or reduced (<5mm).

Dry eye was determined to be present when there were suggestive symptoms along with positive clinical findings and one or more positive tests (tear film break up time of ≤10 seconds, Schirmer test score ≤ 10mm, with anesthesia ≤5mm, fluorescein staining (>5 corneal spots), lissamine green stain (>9 conjunctival spots). A dilated fundus examination was carried out using slit lamp indirect ophthalmoscopy and binocular indirect ophthalmoscopy. Retinopathy when present was classified according to ETDRS guidelines.

Statistical Analysis

IBM SPSS 16 was used for statistical analysis. Descriptive parameters were expressed as mean ±standard deviation, and qualitative variables such as gender, retinopathy, dry eye, corneal sensation etc., were expressed as proportions. Association of retinopathy with other variables was analyzed using Chi-square test of significance. A p value of <0.05 was considered significant.

Results

A total of 81 patients ranging in age from 40-78 years took part in the study; of these 46 were males and 35 were females. The age wise distribution of patients is given in Table 1.

Table 1: Age wise distribution of patients

Age range in years	Number of patients
40-49	24
50-59	22
60-69	30
70-79	5

The overall age wise distribution of dry eye prevalence is given in figure 1, and reduced

corneal sensation in figure 2. Both dry eye and diminished sensitivity correlated with increasing age. ($p < 0.05$)

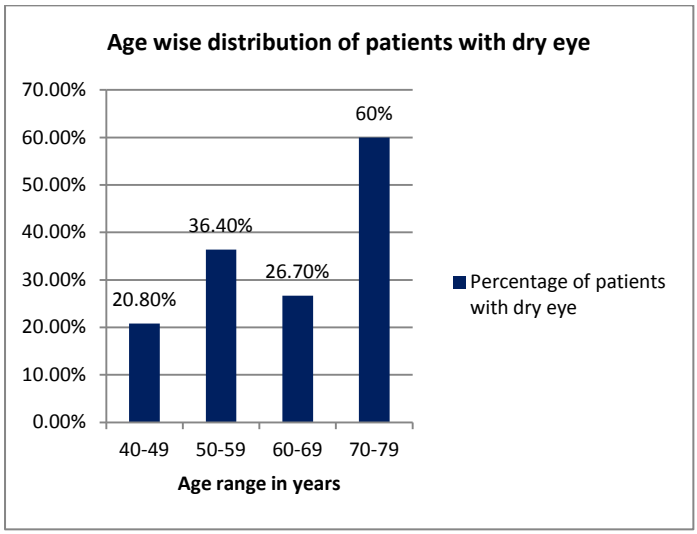

Figure 1 Age wise distribution of patients with dry eye

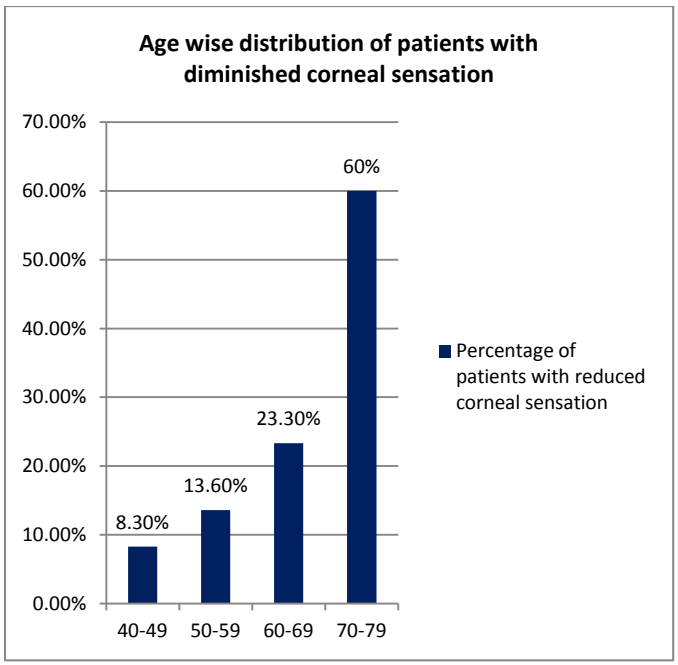

Figure 2: Age wise distribution of patients with reduced corneal sensation

Forty five out of the 81 patients (55.6%) were diabetic. There were 20 males and 16 females among the non-diabetics, and 26 males and 19 females among the diabetic patients. There was a statistically significant association of dry eyes in patients with diabetes (48.9%) compared to 5.6% (2 patients) in non –diabetics ($p<0.0001$). The two patients in the non –diabetic group with dry eyes were both females. The distribution of dry eyes in the diabetic group was roughly equal (twelve males and ten females). The prevalence of dry eye among diabetics was 48.9%.

15 patients out of the total study group of 81 (18.5%) had diminished corneal sensation (Odds ratio= 0.19). Out of these 15, 13 patients (86.7%) were diabetic. All patients with diminished corneal sensitivity had dry eyes ($p<0.0001$). The prevalence of diminished corneal sensation among diabetics was 28.9%.

Out of the 22 patients with dry eye among the diabetics, half of them had retinopathy, four of them mild NPDR, four of them moderate NPDR, two severe NPDR and one PDR.

Out of the 13 patients with diminished corneal sensitivity, 8 (61.5%) had evidence of diabetic retinopathy; four had mild NPDR, three had moderate NPDR, and one had severe NPDR.

The association between dry eye and corneal sensation with retinopathy was not found to be significant.

Discussion

In the present study, there was as significant correlation of type 2 diabetes mellitus with the presence of dry eyes, and with diminished corneal sensation. Neither of these two parameters was found to be correlated with diabetic retinopathy. However these factors were found to be significantly inter related, and both were independently associated with increasing age and duration of diabetes.

Other studies have also found this relation between dry eye and type 2 diabetes. The Beaver dam study cohort found that diabetes was associated with dry eye with an odds ratio of 1.38. The prevalence of dry eye in diabetics in that study was found to be 18.1%.[5] Other studies have also shown an increased prevalence of dry eye in diabetes. [4,9–13]

Autonomic dys regulation,[4] lacrimal gland microvasculopathy, reduced corneal sensitivity, alteration in tear film dynamics and meibomian

gland dysfunction may all contribute to dry eye. [14]

Just as in our study, decreased corneal sensitivity was found to be associated with diabetes in the studies of Dogru et al and Gao et al [7,9,15,16] Neural dysregulation leads to diminished corneal sensation and degeneration of corneal nerve fibres. [7]

Singh et al [17] did not find a statistically increased prevalence of dry eye in their diabetic patients when compared to non-diabetic controls. A small number of patients in each group, and an older age representation in both groups might have led to this outcome.

Duration of diabetes had a significant influence on the prevalence of dry eye and reduced corneal sensitivity in our study. This was consistent with the findings of Manaviat et al, and Shaikh et al. [4,13] who noted a relationship with duration and dry eye. This however was not reflected in the studies of others. [15,18,19] These authors did not study the effect of duration on corneal sensitivity. Gao found a correlation for corneal sensitivity but not dry eye, and Dogru et al did not find a correlation for either dry eye or corneal sensitivity with duration of diabetes.

Unlike our study where we found a significant influence of age on both of these parameters, others did not find such an association. [4,9,18,19]

We did not find any relationship of dry eye or reduced corneal sensitivity to retinopathy, similar to the study of Dogru et al. However, others [11–13] did find an association with dry eye. Manaviat and colleagues found a significantly higher prevalence (59.3 %) of dry eyes in patients with diabetic retinopathy. Nepp [11] and Ozdemir [10] found a greater association with severe forms of retinopathy and with a history of laser treatment. Sheikh and Ameen [13] found a correlation in all stages of retinopathy, with greater prevalence rates in higher grades of retinopathy, similar to that of Li et al,[18] who in addition found a difference between patients with and without a history of photocoagulation.

Gao et al found that both dry eye and diminished corneal sensitivity correlated with proliferative retinopathy. Saito found a correlation of corneal sensation with the stage of retinopathy. and postulated that diabetic retinopathy and polyneuropathy (of which reduced corneal sensation is a manifestation) result from a basement membrane abnormality.

Li et al conducted a meta-analysis on a number of studies involving tear function and corneal sensitivity in diabetes mellitus, and found that there is a greater predisposition for both these conditions in proliferative retinopathy.

The results of our study were consistent with others in terms of prevalence rates of dry eye and diminished corneal sensitivity, but differed with some of them with regard to association with age, duration of diabetes mellitus and with retinopathy. A cross sectional design, and a small sample size could have been the cause of this difference.

Conclusion

There is a generalised agreement regarding the increased prevalence of dry eye and diminished corneal sensitivity in diabetes mellitus. Results with regard to correlations with age, duration of diabetes and retinopathy are varied in different studies. Nevertheless, considering the universal consensus on the problem of ocular surface disease in patients with diabetes mellitus, it is prudent to recommend ocular surface evaluation of all diabetic patients so that institution of appropriate management may be undertaken at the earliest.

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