ORIGINAL RESEARCH PAPER

Ophthalmology

CORRELATION OF DRY EYE SYNDROME IN PATIENTS OF DIABETES MELLITUS ATTENDING A TERTIARY EYE CARE CENTRE.

KEY WORDS: Dry eye, Diabetic Retinopathy, Schirmer's BST, TBUT.

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ABSTRACT

Purpose: To study the correlation of dry eye syndrome in patients of Type 2 diabetes mellitus, attending ophthalmology clinic in Sree Balaji Medical College & Hospital, Chennai.

Materials and Methods: The study involves a hospital based cross-sectional observational study of 100 eyes of 50 patients, aged 50 years & above, diagnosed with Type 2 diabetes mellitus, with or without diabetic retinopathy, on treatment with oral hypoglycaemic agents or Insulin. The parameters evaluated for each patient included a questionnaire (based on Ocular Surface Disease Index (OSDI), Schirmer's Basic Secretion Test (BST) and Tear Film Break Up Time (TBUT) test. All patients underwent routine ophthalmic examination.

Results: The prevalence of dry eye in patients with diabetes is more. The duration of diabetes has direct correlation with the dry eye. Dry eye is more in female sex. Along with that, severity of diabetic retinopathy has direct correlation with the extent of dry eye. These values are also statistically significant (p value <0.001). In patients treated with oral hypoglycaemic agents, prevalence of dry eye is more.

Conclusion: The prevalence and severity of dry eye, based on clinical parameters, was more in patients with diabetic retinopathy as compared to those without diabetic retinopathy. Hence all the diabetic patients coming to ophthalmology out-patient department should be screened for dry eye and treated according to the severity of dry eye.

1. Introduction

Diabetes is a worldwide epidemic affecting a large population of the world. The association of diabetes and dry eye has been observed over the years. Dry eye is 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 increased osmolarity of the tear film and inflammation of the ocular surface.[1] In spite of the fact that this condition rarely leads to loss of vision, it may reduce the quality of life when its symptoms occur. Dry eye is a disorder of the precorneal tear film due to tear deficiency or excessive evaporation which causes damage to the interpalpebral ocular surface and is associated with symptoms of ocular discomfort. Around 5% of urban Indian population suffers from Type 2 diabetes mellitus.[2,3] Approximately 370 million people across the world are expected to be affected by diabetes by the year 2030. According to an Indian study by Khurana et al,[5] dry eye in patients attending ophthalmology OPD based on ocular surface disease index was found to be 29.25% in patients over 40 years of age. [6] The prevalence of diabetic retinopathy in Indian urban population with diabetes mellitus was found to be 18%.[7]

Dry eye is a common ocular condition and a major reason for visits to ophthalmologists. Its prevalence varies widely among epidemiological studies depending on how the disease is defined and diagnosed, and which population is surveyed. It is estimated to be 7.4%–33.7%.[8,9,10] Definitions of the dry eye based on symptoms have been often used to define dry eye prevalence in population-based studies because they are more repeatable and reliable than the objective clinical tests in identifying dry eyes.[11]

While diabetic retinopathy (DR) and diabetic cataracts are well-known complications, dry eye syndrome (DES), also referred to as Keratoconjunctivitissicca, is also common in the diabetic population. Studies have indicated 54% prevalence of asymptomatic and symptomatic DES, in diabetes.[12]

Diabetes mellitus (DM) has been identified as one of the leading systemic risk factors for DES. The reported prevalence of DES in diabetics is 15–33% in those over 65 years of age and increases with age and is 50% more common in women than in men.[13]

2. Classification of Dry Eye Syndrome

DES was recognized as a lacrimal function unit (LFU) dysfunction disease by the International Dry Eye Workshop in 2007. The LFU which protects and maintains the tear film and normal function of the ocular surface is composed of the "cornea, conjunctiva, lacrimal gland, meibomian gland, lids, and the sensory and motor nerves that connect them"[14]. Human tear film comprises three layers: lipid (secreted by the meibomian gland), aqueous (secreted by the lacrimal gland), and mucin (secreted by conjunctiva, cornea, lacrimal gland, and other structures). These three layers contain enzymes, signaling molecules, and metabolites and are essential in maintaining the physiological function of the ocular surface[15].

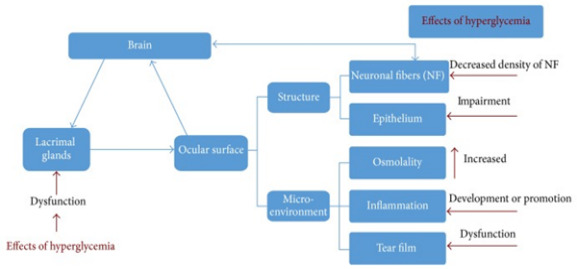
The 1995 NEI/Industry Dry Eye Workshop identified two types of DES: aqueous tear-deficient (tear-deficient, lacrimal tear deficiency) and evaporative dry eye. Aqueous-deficient dry eye has two major subgroups: Sjögren and non-Sjögren syndrome. Evaporative dry eye may be intrinsic (e.g., due to meibomian gland dysfunction, eyelid problems, or low blink rate) or extrinsic (e.g., due to vitamin A deficiency, preservatives in topical medications, contact lens wear, or diseases of the ocular surface)[16]

3. Etiology of Diabetes Mellitus Associated Dry Eye Syndrome

LFU plays a regulatory role in tear secretion and tear film formation and maintains the normal physiology of the ocular surface; damage to any component of LFU leads to tear-deficient or evaporative DES.

Tear hyperosmolarity and tear film instability caused by LFU and ocular surface dysfunction are the key factors in DES. Effects of hyperglycemia on any component of the LFU may be transferred to the entire system via neural connections, leading to insufficient tear production or excess tear loss, abnormalities in blinking, and changes in tear film composition [16]; all these cause DES. The feedback loop for tear secretion and impact of diabetes mellitus on ocular surface and tear production are summarized in Figure 1.

Figure 1:



Lacrimal function unit (LFU) is composed of the "cornea, conjunctiva, lacrimal gland, meibomian gland, lids, and the sensory and motor nerves that connect them," which protect and maintain the tear film and normal function of the ocular **surface.**

4. Lacrimal Functional Unit Dysfunction

Patients with Type 1 or Type 2 Diabetes are at increased risk of developing LFU dysfunction.[17]

DM is a risk factor for corneal epithelial abnormalities. DM causes epithelial barrier dysfunction which subsequently leads to corneal complications and then LFU dysfunction [17]. Diabetes with increased serum HbA1c levels is more predisposed to impaired barrier function in the corneal epithelium [17]. In a diabetic rabbit corneal epithelium dysfunction model, increased levels of glucose, glycogen, and sorbitol have been identified in the diabetic corneal epithelium as compared to controls suggesting that sorbitol pathway activation is involved[18].

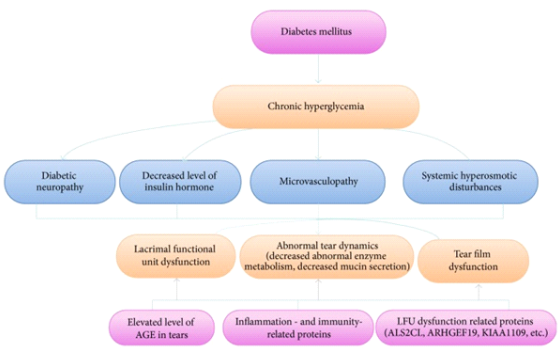
The corneal complications caused by hyperglycemia include superficial punctate keratopathy, trophic ulcers, persistent epithelial defects, and recurrent corneal erosions; all these associated with DES[19]. It has also been shown that diabetics have lower values of tear secretion and tear break-up time test (TBUT).

In aC57BL/6Jdb/db mice model of DMDES, tear production substantially decreased concomitantly with a wounded corneal epithelium. Oxidative stress in the cornea was significantly increased with decreased SIRT1 expression[20].

5. Pathogenesis of DM Associated Dry Eye Syndrome

Chronic hyperglycemia, diabetic periphery neuropathy, decreased insulin levels, microvasculopathy, and systemic hyperosmotic disturbances are risk factors for diabetes-associated DES (Figure 2).

Figure 2:



Chronic hyperglycemia, diabetic periphery neuropathy, decreased insulin hormone, microvasculopathy, and systemic hyperosmotic disturbances are risk factors for diabetes-associated dry eye syndrome**.**

Insulin is critical for proliferation of the acinar lacrimal gland (LG) and cornea epithelial cells. Insulin partially reversed the decreased protein expression induced by LG dysfunction; this process is involved in supporting exocytosis and vesicular formation through insulin replacement therapy[21]. It has been demonstrated that hyperglycemia induces histological alterations in the lacrimal gland, suggesting the role of diabetes-induced oxidative stress in DES[22].

6. Materials and Methods

A total of 100 eyes of 50 patients diagnosed with Type 2 diabetes mellitus were selected from the patients referred to the ophthalmology outpatient department in SBMCH. Gender distribution was 50% male and 50% female. Age of the patients should be more than 50 years to be included in the study. Selection criteria mandated that the patients had to be already diagnosed with diabetes mellitus type 2 and were on treatment with oral hypoglycaemic medications or insulin. 50 patients were asked to answer the OSDI questionnaire and the OSDI scoring was noted. The OSDI questionnaire consists of 12 questions used to give scores in three (vision related, ocular symptoms and environmental trigger) categories. For each subject, sum of scores for all the questions answered is divided by number of questions answered and then multiplied by 25 to give an OSDI score that can range from 0 to 100.Higher OSDI represents greater disability. OSDI>55 is being taken in this study as indicative of diagnosis of dry eye. The duration of diabetes was noted in order to understand the relation between the longevity of diabetes and the dry eye. The 100 eyes of these 50 patients were tested with Schimer's basic secretion test (Schirmers II). The eye is gently dried of excess tears. A drop of local anaesthetic (Proparacaine-0.5%preservative free w/v) was instilled into conjunctival sac in each eye to minimise irritation due to the paper and ensure that only basal secretion of tears is measured. The Schirmer strip(commercially available Whatman filter paper 41 measuring 5 X 35 mm was taken) is folded 5 mm from one end and kept in the lower fornix at the junction of lateral 1/3 and medial 2/3 .The patient is asked to close the eyes. After 5 minutes, the filter paper is removed and the leading edge of wetness measured off the pre-printed scale in mm. A mean value of <10 mm was taken as indicator of dry eye. TBUT test was done in patients who gave<10 mm wetting in their schirmer test. Tear film break up time is time in seconds from the last blink to appearance of first dark spot on the cornea. The lower fornix was stained using pre-sterilised strip of 2% fluorescein. The patient looked straight without blinking while seated on a slit lamp and was observed using broad beam of cobalt blue light. TBUT<10 second was considered abnormal. The patients were then dilated and the fundus details were noted using direct and indirect ophthalmoscopy. The diabetic retinopathy was graded according to the ETDRS scoring (Early Treatment Diabetic Retinopathy Criteria). Statistical analysis was performed with SPSS Version 20.0 statistic software package. Data were expressed as means ± standard deviation (SD). Comparisons between groups were performed with analysis of non-parametric test. A value of $P < 0.05$ was considered statistically significant.

7. Results

The mean age of the 50 patients was taken as 58.9 with SD of 8.7.The sex of the patients is equally divided with male 25 and female 25.Of the 50 patients in the study 32 patients were taking oral hypoglycaemic agents and 18 patients were on treatment with insulin. The duration of diabetes was taken with mean of 4.8 years with SD of 2.6.The grading of retinopathy in diabetes patients was based on ETDRS scoring and there were 23% with mild NPDR, 32 % with moderate NPDR ,26% with severe NPDR and 14% with PDR (Figure1).The Schirmer's test gave values of 17% with <5mm wetting ,38% with 5-10mm,34% with 10-15mm and 11% with >15mm.(Figure2)

Figure1

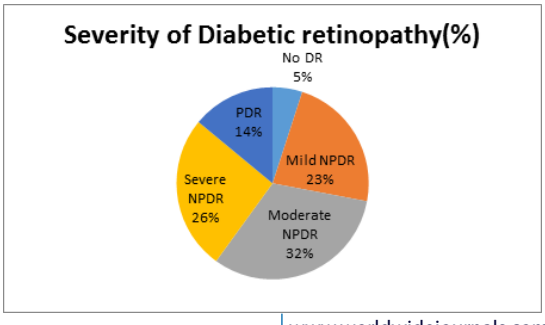


Figure2

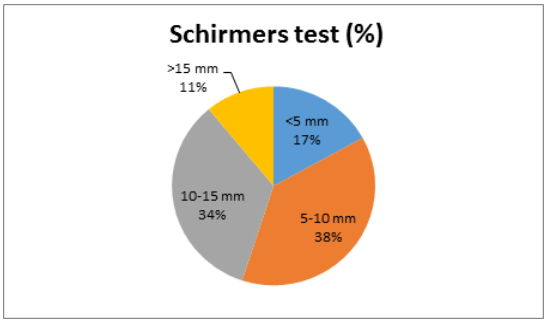


Table 1

	Schirmers Test			
	<5 mm	**5-10 mm**	**10-15 mm**	**>15 mm**
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
Duration of Diabetes (in yrs)	5.5 ± 2.7	5.8 ± 2.6	4.2 ± 2.2	2.3 ± 0.8
p-value	**<0.001 (Significant)**			

Statistical correlation was done using ANOVA test between the duration of diabetes and the severity of dry eye. The result showed a statistically significant correlation with p<0.001.More the duration of diabetes more is incidence of dry eye.

Table 2

Schirmers Test	**Severity of Diabetic Retinopathy**					
	No DR N (%)	**Mild NPDR N (%)**	**Moderate NPDR N (%)**	**Severe NPDR N (%)**	**PDR N (%)**	**Total N (%)**
<5 mm	-	1 (4.3)	5 (15.6)	8 (30.8)	3 (21.4)	17 (17.0)
5-10 mm	-	3 (13.0)	13 (40.6)	13 (50.0)	9 (64.3)	38 (38.0)
10-15 mm	3 (60.0)	13 (56.5)	11 (34.4)	5 (19.2)	2 (14.3)	34 (34.0)
>15 mm	2 (40.0)	6 (26.1)	3 (9.4)	-	-	11 (11.0)
Total	5 (100.0)	23 (100.0)	32 (100.0)	26 (100.0)	14 (100.0)	100 (100.0)
p-value	**<0.001 (Significant)**					

Table 3

	Severity of Diabetic Retinopathy				
	No DR	Mild NPDR	Moderate NPDR	Severe NPDR	PDR
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
OSDI score	33.8 ± 4.3	33.5 ± 12.1	52.1 ± 18.9	57.6 ± 22.4	73.9 ± 7.7
p-value	**<0.001 (Significant)**				

When the severity of diabetes was correlated with the Schirmer's test by Pearsons Chi-square test we found out that moderate and severe NPDR and PDR patients had more dry eye compared to the patients with mild NPDR or no DR. The result was statistically significant (p value <0.001).We also found out that the moderate and severe NPDR and PDR patients had higher OSDI scoring and hence had more dry eye. The data was also statistically significant (p value is <0.001). Amongst the patients we found that female patients had more dry eye compared to male patients and their result had statistical significance (p value of <0.017). More incidence of dry eye was noted in patients on treatment with oral hypoglycaemics but was not statistically significant in our study. There was significant relation between age, sex, duration of diabetes, severity of diabetic retinopathy, OSDI scoring and dry eye in our study.

8. Conclusion

Our sample analysis has led us to the conclusion that prevalence of dry eye syndrome in our study is 55%.The severity of the dry eye was directly related to the duration of diabetes. Dry Eye Syndrome is more prevalent in female sex. Patients with increased severity of dry eye (measured by OSDI scoring, Schirmers and TBUT) were also more likely to have advanced stages of retinopathy.

Hence all the patients with diabetes coming to ophthalmic OPD should be screened and tested for dry eye and treated accordingly.

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