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CORRELATION OF DRY EYE WITH DIABETIC RETINOPATHY IN TERMS OF DURATION, SEVERITY AND GLYCOSYLATED HEMOGLOBIN AT TERTIARY CARE CENTRE

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ABSTRACT **BACKGROUND:** Diabetes Mellitus is one of the most common leading causes of blindness in 20-70 years age group. Recently, problems involving ocular surface, dry eyes in particular, have been reported in diabetic patients. **AIM:** To correlate the Dry Eye with Diabetic Retinopathy in terms of Duration, Severity and Glycosylated hemoglobin at Tertiary Care Centre. **MATERIALS & METHODS:** This prospective randomized study was conducted on 90 patients, between the age group of 40 to 70 years. Patients were divided into three groups, without diabetic retinopathy (N=30), non proliferative diabetic retinopathy (N=30), proliferative diabetic retinopathy (N=30) and 30 healthy controls were included. Variables parameters were age, gender, duration of diabetes, glycosylated hemoglobin, Schirmer test, Tear Breakup Time (TBUT),Tear meniscus height (TMH), and dry eye symptoms. All results were analysed using appropriate statistical tests. **RESULTS:** Dry eye significantly correlate with Severity of Diabetic Retinopathy (p=0.000), Dry eye test like Schirmer test , TBUT, TMH showed significant results (p=0.000), Dry eye symptoms significantly increases with Duration and Glycosylated hemoglobin (p=0.000). **CONCLUSION:** Diabetic patients are more prone to develop dry eye symptoms as compare to normal subjects. Dry eye assessment should be mandatory in every patient of diabetes, to diagnose the complications of dry eye and treat accordingly as early as possible.

KEYWORDS : Diabetic Retinopathy (DR), Dry Eye, Schirmer test, Tear Breakup Time (TBUT), Tear meniscus height (TMH)

INTRODUCTION

Diabetes is one of the leading causes of morbidity and mortality globally [1]. In 2017, 425 million people were diagnosed with diabetes globally and this figure is expected to exceed 629 million by 2045 [2].

In 2007, the International Dry Eye Workshop updated the original definition and classified dry eye as "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 increased osmolarity of the tear film and inflammation of the ocular surface" [3]. Diabetes patients are more prone to develop the dry eye symptoms as compare to non-diabetic subjects. Diabetic patients might exhibit dry eye symptoms probably due to neuropathy, metabolic dysfunction or abnormal lacrimal secretions [4]. Aldose reductase, the first enzyme of the sorbitol pathway may also involved. The oral administration of aldose reductase inhibitors has been shown to improve the tear dynamic significantly [5].

Patients who have dry eye often complain of eye irritation, gritty or foreign body sensation, burning, tearing, photophobia, stinging and intermittent sharp pain. Blurred vision that improves with blinking or instillation of nonviscous artificial tears is also common.

Ocular surface disease in diabetes is characterized by reduced corneal sensitivity and by alteration in tear quantity and quality [6]. Therefore early diagnosis of dry eye symptoms in diabetic patients is important for beginning of treatment in early stages.

This study conduct to find out the Correlation of Dry Eye with Diabetic Retinopathy in terms of Duration, Severity and Glycosylated hemoglobin.

MATERIAL & METHODS

This prospective randomized study was carried out on patients of Department of Ophthalmology at Mathura Das Mathur combined Hospital with Dr. S.N. Medical College, Jodhpur, Rajasthan from August 2018 to July 2019. Patients in the age group 40 to 70 years were included. 90 consecutive cases of type 2 diabetes mellitus were divided into three groups: patients of diabetes without retinopathy (No DR; n = 30); non-proliferative diabetic retinopathy (NPDR; n = 30) and proliferative diabetic retinopathy (PDR; n = 30) on the basis of ETDRS classification. Thirty age and sex matched healthy controls were included. Subjects with ocular surface diseases and systemic disease which known to cause dry eye other than diabetes mellitus, patients who are on local and systemic medications which are known to cause dry eye, contact lens users, glaucoma, any previous eye infection or inflammation, any previous intraocular surgery, any ocular trauma were excluded.Carl Zeiss Meditec Inc. 5160 Hacienda Drive Dublin, CA 94568

Written informed consent was taken from all the participants in the study. Patient data regarding dry eye was collected in terms of age, gender, locality, presenting symptoms, duration, progression and associated conditions. Furthermore history of Diabetes Mellitus, treatment duration and blood reports of fasting, post prandial blood sugar and glycosylated hemoglobin was recorded.

Brief general systemic examination and detailed ophthalmic examination was done including best corrected visual acuity (BCVA), intraocular pressure (IOP), slit lamp examination for anterior segment to know the condition of eyelid, meibomian gland, conjunctival surface and cornea and dilated fundus examination with direct and indirect ophthalmoscopy.

Tear film evaluation was done in the following order.

Tear meniscus height (TMH) was recorded as normal or low under slit lamp, precorneal tear film was observed for debris.

Schirmer's Test

Filter paper is placed in the inferior cul-de-sac from outer one-third and inner two-third and the amount of wetting of the paper strip after 5 min was measured. Normal value of Schirmer I test are more than 15 mm. Wetting of 5-10 mm was taken as moderate and <5 mm is severe.

Tear Breakup Time (TBUT) Measurement

A dry fluorescein strip is touched to the inferior fornix with patient instructed to look up. The corneal surface is seen under slit lamp with low magnification using a cobalt blue filtered light. The patient is asked to blink ones and look straight without blinking. The time of appearance first small black spot within blue field (dry spot) from last blink measures the tear film. TBUT <10 s are taken as abnormal.

Statistical Analysis

All statistical analysis was done with the help of SPSS software. Data has been summarized and presented as Mean ± SE. The continuous

variables of the study groups were compared by one factor analysis of variance (ANOVA). The discrete (categorical) variables were compared by chi-square ($\chi 2$) test. P value less than 0.05 was considered statistically significant.

RESULTS

The mean age in years was 52.46±2.19 in controls, 54.06±2.13 in No DR group, 56.10±1.09 in NPDR and 58.90±2.00 in PDR group (p=0.22). The gender distribution among study groups was found to be 17 males and 13 females in control group, 10 males and 20 females in No DR group, 13 males and 17 females in NPDR and 14 males and 16 females in PDR group. Chi square revealed similar gender distribution among the groups (p=0.33). The mean duration of diabetes mellitus in years was 4.53±0.97 in No DR, 10.06±2.03 in NPDR and 13.4±1.42 in PDR. A significant difference was observed among the three groups (p=0.000). Other variables like glycosylated hemoglobin (HbA1c), Schirmer test, Tear break up time (TBUT), Tear meniscus height (TMH), Symptoms of dry eye among the study groups have been summarized in Table 1.

Table 1- Summary of various parameters (mean±SE) among the study groups

Variables (Mean±SE)	Controls	No DR	NPDR	PDR	p value
Age (years)	52.46±2.19	54.06±2.13	56.10±1.09	58.90±2.00	0.22
Gender Male Female	 17 (14.16%) 13 (10.83%)	 10 (8.33%) 20 (16.66%)	 13(10.83%) 17(14.16%)	 14(11.66%) 16(13.33%)	 0.33
HbA1c (%)	5.24±0.056	7.23±0.112	7.71±0.152	8.28±0.100	0.000*
Duration of diabetes (years)	--	4.53±0.97	10.06±2.03	13.4±1.42	0.000*
Schirmer test Normal (>15mm) Mild (10-15mm) Moderate (5-10mm) Severe (<5mm)	 30 (25%) - - -	 24 (20%) 6 (5%) - -	 - 16 (13.33%) 14 (11.66%) -	 - 2 (1.66%) 24 (20%) 4 (3.33%)	 0.000*
Tear Breakup Time (TBUT) Normal (>10s) Low (<10s)	 30 (25%) -	 28 (23.33%) 2 (1.66%)	 10 (8.33%) 20(16.66%)	 2 (1.66%) 28(23.33%)	 0.000*
Tear meniscus height (TMH) Normal Thin Absent	 30 (25%) - -	 26 (21.66%) 4 (3.33%) -	 10 (8.33%) 18 (15%) 2 (1.66%)	 4 (3.33%) 18 (15%) 8 (6.66%)	 0.000*
Based on Symptoms No dry eye Dry eye	 30 (25%) -	 16 (13.33%) 14 (11.66%)	 6 (5%) 24 (20%)	 2 (1.66%) 28(23.33%)	 0.000*

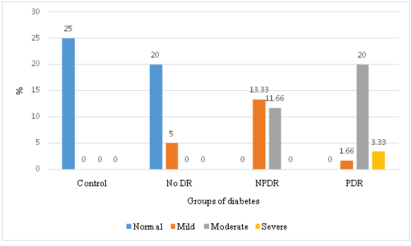

Figure 1: Schirmer test among the study groups

In figure 1 schirmer test grading was significantly correlate with the severity of Diabetic Retinopathy(DR) (p=0.000). Normal (20%) and mild (5%) grades of schirmer test were found in No DR group, Mild (13.33%) and moderate (11.66%) grades were found in NPDR group, mild (1.66%), moderate (20%), severe (3.33%) grades were found in PDR group.

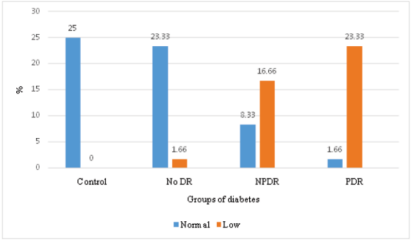

Figure 2: Tear break up time (TBUT) among the study groups

In figure 2 Tear Breakup Time (TBUT) was significantly correlate with the severity of DR (p=0.000). TBUT was normal (23.33%) and low (1.66%) in No DR group, normal (8.33%), and low (16.66%) in NPDR group, normal (1.66%) and low (23.33%) in PDR group.

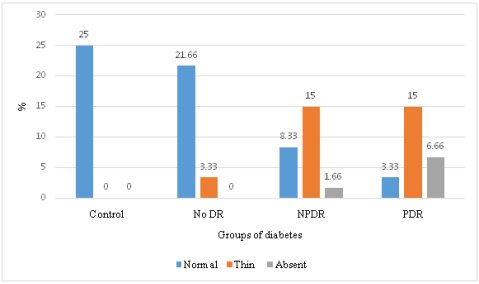

Figure 3: Tear meniscus height (TMH) among the study groups

In figure 3 Tear meniscus height (TMH) was significantly associate with severity of DR (p=0.000). TMH was normal (21.66%) and thin (3.33%) in No DR group, normal (8.33%), thin (15%) and absent (1.66%) in NPDR group, normal (3.33%), thin (15%) and severe (6.66%) in PDR group.

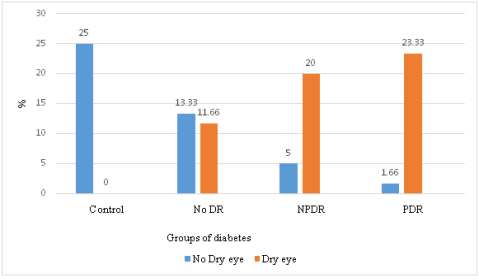

Figure 4: Symptoms of dry eye among the study groups

In figure 4 symptoms of dry eye were found statistically significant with severity of DR (p=0.000).Dry eye symptoms were found (11.66%) in No DR group, 20% in NPDR group, 23.33% in PDR group.

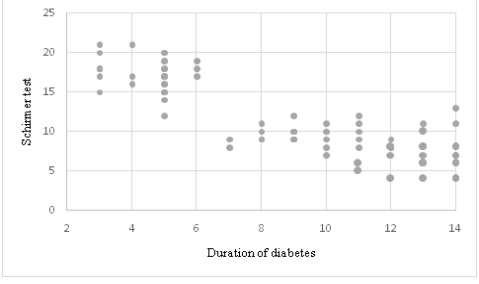

Figure 5: Scatter plot between schirmer test and duration of diabetes

Figure 5 showed that schirmer test grading were progressed normal to severe with duration of diabetes, that indicated that dry eye significantly increases with the duration of diabetes (p=0.000).

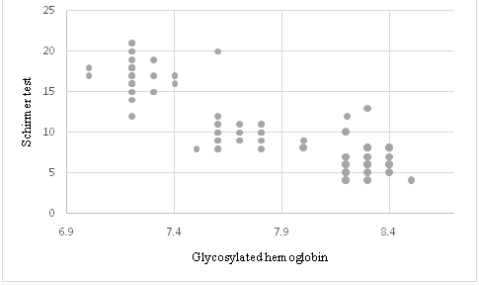

Figure 6: Scatter plot between schirmer test and glycosylated hemoglobin

Figure 6 showed that shirmer test grading were progressed normal to severe with hyperglycemia, that indicated that dry eye significantly

increases with high level of glycosylated hemoglobin.

DISCUSSION

Dry eye is a multifactorial disease. Diabetic patients are more predisposed to tear film instability and reduced tear secretions. Diabetic cornea has higher chances to decompensate following stress.

In present study, mean age (in years) of control was 52.46±2.19, 54.06±2.13 in No DR, 56.10±1.09 in NPDR and 58.90±2.00 in PDR. Our study like Kaiserman et al [7] showed that prevalence of dry eye increases with age.

The duration of diabetes (in years) was 4.53±0.97 in controls, 10.06±2.03 in NPDR and 13.4±1.42 in PDR. Our study showed significant correlation of dry eye symptoms with duration of dry eye (p=0.000). Mean value of glycosylated hemoglobin was 5.24±0.056 in controls, 7.23±0.11 in No DR, 7.71±0.15 in NPDR and 8.28±0.10 in PDR. Our study showed the dry eye was significantly increases with severity and glycosylated hemoglobin (p=0.000), like Nepp et al [8] were able to correlate the severity of retinopathy with the severity of dry eyes. KC Yoon et al [9] suggest that poor metabolic control, presence of Diabetic Retinopathy stages is risk factors for tear film and ocular surface disorder in Diabetes Mellitus.

In our study the Schirmer test I and TBUT was significantly correlate with severity of diabetes. Normal (20%) and mild (5%) grades of schirmer test were found in No DR group, mild (13.33%) and moderate (11.66%) grades were found in NPDR group, mild (1.66%), moderate (20%), severe (3.33%) grades were found in PDR group. TBUT was normal (23.33%) and low (1.66%) in No DR group, normal (8.33%, and low (16.66%) in NPDR group, normal (1.66%) and low (23.33%) in PDR group. In Goebels et al [10] Schirmer test and tearing reflex was significantly lower in diabetic patients compared with control group. In Jin et al [11] TBUT was significantly lower in type 2 diabetic patients. Similar study Ozdemir et al [12] concluded that TBUT and Schirmer test values were significantly lower in diabetic patients compared with controls (p<0.001).

In our study, TMH was normal (21.66%) and thin (3.33%) in No DR group, normal (8.33%), thin (15%) and absent (1.66%) in NPDR group, normal (3.33%), thin (15%) and severe (6.66%) in PDR group. Dry eye symptoms were found (11.66%) in No DR group, 20% in NPDR group, 23.33% in PDR group.Whitcher et al [13] found a scanty or absent meniscus is an indicator of aqueous tear deficiency, In this study TMH was thin 49% and absent in 13%.

Dry eye symptoms tend to be more reliable and accurate than clinical test for dry eye. In our study, we have made the diagnosis of dry eye based on symptoms, sign and diagnostic tests which included Schirmer test, TBUT and TMH. We observed in our study that a large number of patients had no symptoms or signs of ocular surface damage had abnormal TBUT, TMH and Schirmer test values.

CONCLUSION

Dry eye significantly increases with severity, duration and glycosylated hemoglobin in patients of Diabetic Retinopathy. Schirmer test, TBUT, TMH and other test of dry eye should be mandatory in diabetic patients. Early diagnosis of dry eye symptoms in diabetic patients is important for the beginning of treatment in early stages.

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