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Original Research Article

Correlation of dry eye and diabetes mellitus

Saura Kamal Dutta[1],*, Gautam Paul[1], Gaurav Paul

[1] *Dept. of Ophthalmology, Silchar Medical College and Hospital, Silchar, Assam, India*

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ABSTRACT

Background: Diabetes is one of the leading causes of morbidity and mortality worldwide and various studies have shown that people with diabetes are more prone to suffer from dry eye disease than those without diabetes. This study was undertaken with the aim to find the prevalence of dry eye disease in patients of type 2 diabetes mellitus and to find the correlation between glycemic control and prevalence of dry eye.

Methods: This study was carried out over a period of one year and cases of type 2 diabetes were selected from patients attending the out patient department. Diagnosis of dry eye was made if OSDI Score was more than 12 with one of the positive specific tests for dry eye.

Results: A total of 180 eyes of 100 patients were included in the study. It was noted that with increasing age the chance of dry eye increase. Our study found that with increased duration of diabetes, the chance of developing dry eye increases, and poor glycemic control increases the severity of dry eye. The severity of diabetes has a positive correlation with goblet cell loss and morphological changes in conjunctival impression cytology.

Conclusion: It is established in our study that there is a positive correlation between prevalence of dry eye and poor glycemic control in a patient of diabetes. Since, the prevalence of dry eye in a hospital-based study with limited sample is significant hence the prevalence in the community must be higher and needs attention.

1. Introduction

Diabetes is one of the leading causes of morbidity and mortality worldwide and around 425 million people were diagnosed with diabetes globally, and this figure is expected to exceed 629 million by 2045.[1] As per various studies, people with diabetes are more prone to suffer from dry eye disease than those without diabetes.[2–6] Dr eye disease (DED) is defined as a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film accompanied by ocular symptoms, in which tear film hyperosmolarity, instability, ocular surface damage and inflammation, and neurosensory abnormalities play etiological roles.[7] Dry eye disease has a significant impact on patient's quality of life (QoL) including physical, social, psychological, negatively affecting daily activities and workplace productivity. DED has a substantial economic impact as a result of these QoL effects.[8,9] This study is conducted to find the prevalence of dry disease in patients of type 2 diabetes mellitus and to find the correlation between glycemic control and prevalence of dry eye.

2. Materials and Methods

The clinical observational study was conducted for a period of one year starting from June 2019-May 2020. All the patients with type 2 diabetes mellitus fulfilling the inclusion and exclusion criteria over the study period was included in the study and received a detailed workup.

Inclusion criteria was all diagnosed cases type 2 of diabetes mellitus of either sex if they were in age group

* *Corresponding author*.
E-mail address: saurakamal20@gmail.com (S. K. Dutta).

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of 35-70 years. Subjects with secondary diabetes and those who are on other non-diabetic medications that could affect tear production were excluded from the study. Previous history of ocular surgery, persons with Bell's palsy, Sjogren's syndrome, rheumatoid arthritis, or parkinson disease were excluded.

Written informed consent was taken before enrolling the patients in the study. Type II diabetic patients diagnosed by the American Diabetes Associations criteria.[10,11] The duration of diabetes, fasting and post-prandial blood sugar and Hb1Ac values were recorded.

An ocular surface disease (OSDI) questionnaire was administered to all participants to assess the symptoms of dry eye and correlate them with the signs. A complete ocular examination of the lid margins, conjunctiva, cornea and tear film was done. Examination of fundus was done to access the grade of diabetic retinopathy in the patients. Relevant examination of other important ocular structures was done. Following this, tests to diagnose dry eye were performed. These are tear break up time (TBUT), Ocular surface staining by Rose Bengal and fluorescein staining, Schirmer's tests and conjunctival impression cytology.

Tear film break up time (TBUT) is the time in seconds between the last blink and the appearance of the dry spot. After instilling a drop of 2% fluorescein into the right eye, the patient was asked to blink a few times and place his head in the slit lamp. Then he/she was asked to look straight ahead without blinking. The tear film was observed, watching for an area of tear film rupture manifested by Black Island within the green sea of fluorescein. The time elapsed between the last blink and appearance of first black spot was termed as tear film break up time and noted in seconds. This kind of measurement was taken for three successive blinks and the mean of this was noted as the final reading. Break up time of less than 10 seconds was considered positive, indicative of dry eye. Greater than or equal to 10 seconds was considered negative.

Ocular surface staining is a measure of assessing ocular surface damage using sodium fluorescein or rose Bengal. Staining of the cornea is done by first placing a drop of sterile saline on a sterile fluorescein strip. The fluorescein strip is then placed in the inferior cul de sac of the eye by pulling down on the lower lid and then gently touching the bulbar conjunctiva with the fluorescein strip. The eye was examined for staining of cornea and conjunctiva using cobalt blue filter of slit lamp. Optimal viewing is between 1 and 3 min after instillation. A positive result is > 5 corneal spots.

Similarly, rose Bengal strip is then placed in the inferior cul de sac and after 15 seconds, this eye was examined for staining of cornea and conjunctiva.

Schirmer's test was performed before the other tests as it had to be done before instillation of anaesthesia. It was done using 5×35mm sterile strips of Whatman No.41 filter paper. Patient was made to sit in relatively dark room with fan switched off. The terminal round end of the strip was folded at the pre marked area. The patient was then asked to look up, lower lid retracted and the test paper inserted in the lower cul de sac at the junction of medial 2/3rd and lateral 1/3rd of the lid. Adequate care was taken during the procedure to ensure that the paper did not touch cornea, in order to avoid reflex tearing. The patient was advised to blink normally. At the end of 5 minutes, the strips were removed and the length of filter paper moistened was measured in mm starting from the fold. More than 10mmof wetting after 5 min was considered normal, 8–10mm of wetting was considered mild dryness, 5–7mm of wetting was considered moderate dryness, and less than 5mm of wetting was considered severe dryness at the end of 5 min.

Conjunctival impression cytology was conducted using cellulose acetate strips having a pore diameter of 0.45μm cellulose that were cut into wedge shaped pieces. The patient was lied in supine position, a drop of proparacaine hydrochloride 0.5% was instilled into the eye. After inserting a wire speculum, the wedge shaped filter paper strips was applied on the temporal bulbar conjunctiva with the help of a blunt smooth edged forceps. A smooth glass rod was used to press the paper gently. The strip was then removed with a peeling motion after 2-3 seconds. The strips were gently pressed over clean glass slide and the slides were fixed with 95% ethanol till further staining. Four such impressions were taken for each patient, two for each eye. The slides were stained using PAS stain and H and E stain. The epithelial cell morphology and Goblet cell counting was done to grade them according to standard criteria proposed by Nelson.[12]

Statistical analysis- The data hereby collected was documented on a master chart in MS Excel 2016. These were compiled, tabulated and put into charts. The 'p value' less than 0.05 was considered statistically significant.

3. Results

A total of 100 patients fulfilled the criteria and total 180 eyes is included in the study. The 20 eyes of those patient were excluded from the study due to history of ocular surgery. The age group of the patient included in the study was 35-70 years mean age being 54.52 years. It was noted that with increasing age the chance of dry eye increases. The finding was statistically significant. The male and females were almost equal that is 51 and 49. Prevalence of dry eye in diabetes in males and females were comparable to each other that is 45.09% and 55.10%. The difference in prevalence between male and female is statistically not significant.

The most common symptoms that the patient presented were increased frequency of blinking, itching, and eye fatigue. The Ocular Surface Disease Index (OSDI) questioner was given to every patient and score was

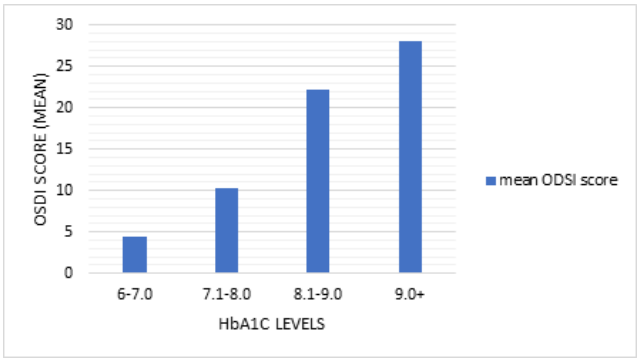

Fig. 1: HbA1c and OSDI score

recorded. On plotting the OSDI score to the HbA1c level it was found that the diabetics with high HbA1c levels had increased OSDI score implying more severe symptoms (Figure 1).

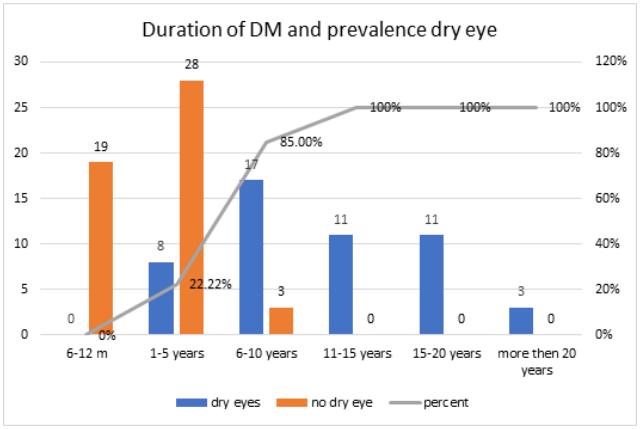

Fig. 2: Duration of diabetes and prevalence of dry eye

In our study most participants were in the range 6-10 years and it was found that with increased duration of diabetes the chance of developing dry eye increases. This can be appreciated in the Figure 2.

Our study showed that the number of eyes with the Schirmer score more than 15 mm was 64, between 10-15 and 5-10 was 49 and 42 respectively, and below 5 mm there were 25 eyes. A statistically significant co-relation was found on comparing between Schirmer score of that eye and HbA1c level of that individual.

In this study out of 180 eyes there were 39(21.67%) eyes had retinopathy. Twenty eyes had mild NPDR, 13 had moderate NPDR, 3 had severe NPDR and 3 had PDR. All the patient with severe NPDR and PDR had Schirmer score of below 5 mm.

In eyes with Schirmer score less than 5mm the mean FBS was 229.2 mg/dl, mean PPBS was 365.8 mg/dl and mean HbA1c was 10.4%, these values shows marked derangements in glycemic control in those patients. This is in contrast to eyes whose Schirmer test score was more than 15 mm with mean FBS, PPBS and HbA1c were 138.97 mg,220mg and 6.88% implying a better glycemic control.

Out of 180 eyes, 78 had tear film break up time less than 10 seconds, while 102 eyes had more than 10 seconds. And majority of eyes with poor glycemic control had positive TBUT result.

Out of 180 eyes, 56 had showed staining with rose Bengal with score 4 or more, while 102 eyes had no stains or a score of less than 4. The mean HbA1c levels of patients having a positive rose Bengal test was 9.07 while of those with negative results was much lower 7.1.

Out of 180 eyes, 60 had showed staining with fluorescein, while 120 eyes had no stains or less than 5 corneal spots. The mean HbA1c levels of patients having a positive rose Bengal test was 8.9 while of those with negative results was much lower 7.1.

Out of 180 eyes examined, 110 did not show any metaplasia, while 50 showed grade 1 changes, 18 showed grade2 changes and only 2 showed grade 3 changes.

4. Discussion

A total of 100 diabetic patients and 180 eyes were included in the study. The 87 eyes of those patient were diagnosed to have dry eye. The prevalence of dry eye in this study was found to be 48.33%.

The studies on diabetic patients showed increased prevalence of dry eye like Manaviat et al.[13] showed 54% of those with diabetes had dry eye while Hom and De Land[14] did a study on patients with either diabetes or borderline diabetes and found that 53% of patients presented with dry eye. But our findings differ from that of Kaiserman et al.[15] (20.6% prevalence) as they determined DED by ocular lubrication use.

The total patient sample was divided into 6 subgroups based on their age. The mean age was 54.52 years. The prevalence of dry eye was found to significantly increase with increase in age of the patients. This finding was statistically significant with p value of 0.0000006. This finding of our study corresponds to the study by Moss et al.[16] which showed an association between older age and an increase in dry eye symptoms.

We found a higher prevalence of dry eye in women, compared to men, but the difference was statistically not significant as p value was more than 0.05 that is 0.563668. This finding has corresponded to the findings of other studies. Moss et al.[16] found a prevalence of 16.7% in women compared to 11.4% in men. Sahai et al.[17] found prevalence of 22.8% in women compared to 14.9% in men in his study on hospital based population.

Increased frequency of blinking was most common symptoms with which our patients presented similar to Schlote et al.,[18] who reported distinct patterns of eye blinking in patients with moderately dry eyes.

Table 1: Retinopathy, HbA1c levels andschirmer's test

		Schirmer score 15+	Schirmer score 10-15	Schirmer score 5-10	Schermer score below 5
HBA1C	Less than 7%	39	10	3	1
	7.1-8.0%	23	28	17	9
	8.1-9.0%	2	3	15	5
	More than 9%	0	8	7	10
	P value	0.000000000041			
Retinopathy	No	62	39	28	12
	Mild NPDR	2	6	9	3
	Moderate NPDR	0	4	5	4
	Severe NPDR	0	0	0	3
	PDR	0	0	0	3
	P value	0.0000002			

Table 2: Rose Bengal test, TBUT, and HbA1c levels

	TBUT				Rose Bengal Test			
HBA1C	**Positive**	**Negative**	**Total**	**P value**	**Positive**	**Negative**	**Total**	**P value**
Less than 7%	4	49	53		0	53	53	
7.1-8.0%	28	49	77	0.000124	11	66	77	0.000000289
8.1-9.0%	21	4	25		20	5	25	
More than 9%	25	0	25		25	0	25	
Total	78	102	180		56	124	180	

Table 3: Fluorescein test, Impression cytology and HbA1c levels

	Fluorescein test				Impression cytology					
HBA1C	**Positive**	**Negative**	**Total**	**P value**	**Grade 0**	**Grade 1**	**Grade 2**	**Grade 3**	**Total**	**P value**
Less than 7%	0	53	53		53	0	0	0	53	
7.1-8.0%	14	63	77	0.0000000002101	57	20	0	0	77	0.00000000001
8.1-9.0%	21	4	25		2	15	8	0	25	
More than 9%	25	0	25		0	13	10	2	25	
Total	60	120	180		110	50	18	2	180	

In our study, as per the OSDI score we found 92 eyes (51.11%) did not have dry eye, 58(32%) eyes had mild dry eye and 20 (11.11%) moderate dry eye while 10 (5%) eyes had severe dry eye. This is similar to Ibtesam Nasimul Hasan et al.[19] who did a study in India in 2014 and also matching the data reported by study conducted by Aggarwal et al.[20]

OSDI scores were found to correlate positively with HbA1c levels in our study that is with increase in HbA1c levels there is increase in OSDI scores. Our observations are in line with previous studies elsewhere, which have shown a positive correlation between OSDI scores and glycemic control. K Divya et al.[21] in their study conducted in India on 2016-2017 also found positive correlation between OSDI Score and HbA1clevels in study population. S. Kan et al.[22] in their study in Turkey in 2016 concluded that diabetes appears to cause elevation in OSDI score and increase in Tear Film Osmolarity level, especially if blood glucose is poorly regulated.

Positive correlation was found between duration of diabetes and prevalence of dry eye in our study and this was statistically significant with a p value 0.000001. Association between duration of diabetes and dry eye has been established in some studies like by Manaviat et al.,[13] and Zhang et al.[23] Some studies also show no correlation between duration and dry eye like studies by Dogru et al.[24] and Ozdemir et al.[25]

In our study we find that with increase in HbA1c levels the Schirmer values decreases. That means there is a inverse correlation between glycemic control and Schirmer test values.

This finding is in correlation with most of the studies in the past some of which include study by Goebbels et al.,[26] Dogru M et al.,[24] Ozdemir M et al.,[25] Gupta I et al.,[27]

and Divya K et al[21] all of these studies has reported that Schirmer test values decrease in diabetic patients more so in patients with poor glycemic control.

In our study we find that patients with advanced stages of retinopathy had higher chances of developing dry eye. This finding was statistically significant and is in line with studies conducted in the past. Studies by J. Nepp et al.[28] R. L. McKown et al.,[29] Ozdemir M et al.,[25] and Zhang X et al.[23] have demonstrated a positive correlation between retinopathy and dry eye.

In our study we have found that the patients whose eyes had a Schirmer score less the 5 mm had a poorer glycemic control then those with scores more than 15 mm. This establishes the fact that the poorer the glycemic control the more is the chance of dry eye. This result was in accordance with other reports like U. Seifart and I. Strempel,[30] Ozdemir M et al.,[27] Najafi L et al.[31] and Zou X et al.[32]

In our study we have found that all the patients with more than 9 HbA1c levels had TBUT less than 10 seconds and patients who had more HbA1c levels had a higher chance of having less tear film break up time.

This finding is supported by the studies conducted by Dogru M et al.,[24] Gupta I et al.,[27] Divya K et al.[21] who had evaluated the tear film and ocular surface changes among diabetics from various parts of India.

Significant staining of the ocular surface with fluorescein and rose Bengal was noted in diabetic patients in our study. Impaired corneal epithelial barrier function in diabetic patients has been reported by several studies like by Gekka M et al.,[33] Ozdemir M[25] and Yoon KC et al.[34] and poor metabolic control and advanced retinopathy have been found to correlate with epitheliopathy.

Our impression cytologic analysis showed a higher grade of squamous metaplasia and lower goblet cell density in the diabetic patients. Epithelial cells were larger and more polygonal and the nucleocytoplasmic ratio was increased. In severe cases multinucleated variable staining cytoplasms and small nuclei even pyknotic or absent nuclei were found. Most of the previous studies have suggested that impression cytology is altered in the diabetic cases like studies by Dogru M,[24] Yoon et al.,[34] Nepp et al.,[35] and Inoue et al.[36]

5. Conclusion

In this study, we find a significant correlation between the prevalence of dry eye in the diabetic patient which shows poor glycemic control is directly related to dry eye. In this study we had taken diabetic patients attended in our hospital who were screened for dry eye and found that a considerable proportion of patients had dry eye. This puts emphases on the fact that if the prevalence of dry eye in a hospital-based study with limited sample is significant then the prevalence in the community must be higher and needs attention.

6. Source of Funding

None.

7. Conflict of Interest

The authors declare that there is no conflict of interest.

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Author biography

Saura Kamal Dutta, Post Graduate Student

Gautam Paul, Associate Professor

Gaurav Paul, General Practitioner

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